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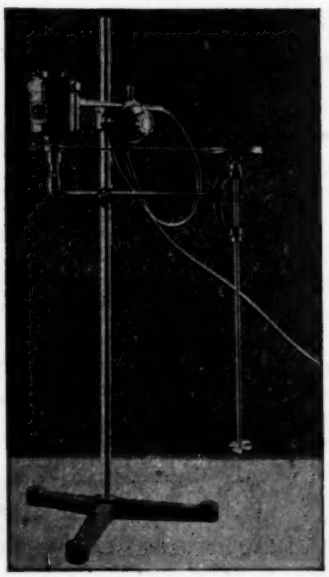

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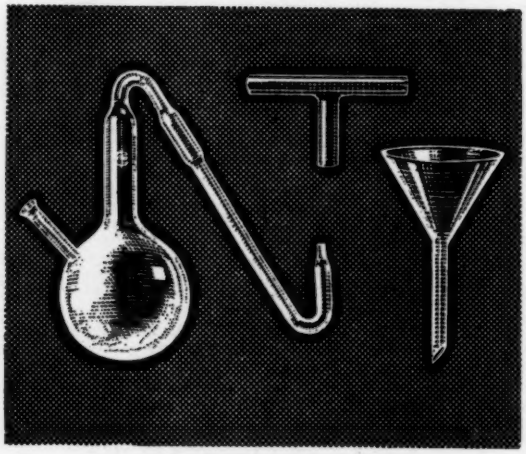

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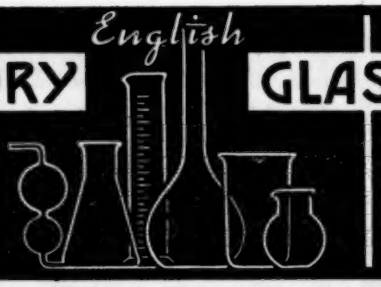

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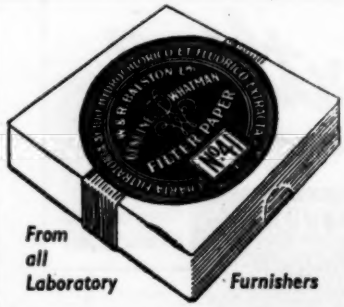

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1 : 2-*benzacridone*, m. p. 334°, pale yellow needles from aqueous pyridine (Found : N, 4·75%), and 5′ : 6-dimethyl-3 : 4-dihydro-1 : 2-benzacridone (0·4 g.) yielded 0·05 g. of 5′ : 6-*dimethyl*-1 : 2-*benzacridone*, m. p. 276°, pale yellow needles from 50% pyridine (norit) (Found : N, 5·0%).

My thanks are due to the Directors of Messrs. Hopkin and Williams Ltd. for facilities and for permission to publish these results.

RESEARCH LABORATORY, HOPKIN AND WILLIAMS LTD., LONDON, E.C. 1. [*Received, October 17th*, 1944.]

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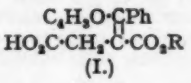
48. *Intramolecular Ring Closures with* cis- *and* trans-*γ-Phenyl-γ-(2-furyl)itaconic Acid.**

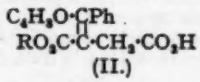
By EDWARD B. KNOTT.

cis- and trans-*γ-Phenyl-γ-(2-furyl)itaconic acid* have been prepared by the condensation of ethyl succinate with phenyl 2-furyl ketone. The *cis*-acid has been cyclised to 4-*hydroxy*-7-*phenylcoumarone*-2-*carboxylic acid* and 1-*keto*-3-(2′-*furyl*)*indene*-2-*acetic acid*, both of which give 2-*hydroxy*-9-*keto*-3′ : 2′ : 3 : 4-*furofluorene* on further cyclisation. The *trans*-acid underwent ring closure to 1-*hydroxy*-4-(2′-*furyl*)*naphthalene*-3-*carboxylic acid*.

THE synthesis of 1-hydroxy-4-phenylnaphthalene-3-carboxylic acid was effected by Borsche and his school (*Annalen*, 1936, **526**, 1) by intramolecular ring closure of the monoester of γγ-diphenylitaconic acid. The cyclisation of the dibasic acid was achieved by Stobbe and Vieweg (*Ber.*, 1902, **35**, 1727), who obtained 1-keto-3-phenylindene-2-acetic acid, which was cyclised by Borsche (*loc. cit.*) to 2-hydroxy-3 : 4-benzfluorenone. This fluorenone has now been found to function as a colour coupler, giving on development of a photographic emulsion with dialkyl-*p*-phenylenediamines a black dye image. It was thought to be of interest, therefore, to prepare other fluorenones of this type.

This work follows the same line of reactions as the above, but by the replacement of one of the phenyl groups of the itaconic acid by a furyl group, two isomeric itaconic acids were to be expected which could lead to two series of cyclisation products. The initial materials were obtained by the condensation of phenyl 2-furyl ketone with ethyl succinate under the influence of alcoholic sodium ethoxide. Depending on the conditions of condensation, two isomeric products were isolated, *ethyl hydrogen* cis-*γ-phenyl-γ-(2-furyl)itaconate* (I; R = Et) and the trans-*isomer* (II; R = Et).


(I.)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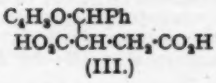
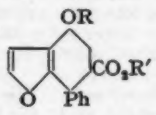

(III.)

Hydrolysis of these products yielded cis- and trans-*γ-phenyl-γ-(2-furyl)itaconic acids* (I and II; R = H). On reduction with sodium amalgam the acids yielded what are believed to be the isomeric forms of *γ-phenyl-γ-(2-furyl)pyroracemic acid* (III). This acid contains two asymmetric carbon atoms and can give two racemates.

The analysis of the acids indicates in both cases the presence of water of crystallisation, which is difficult to remove. The addition of elements of water to the furan ring during reduction, leading to an aldehyde, is unlikely, as the acids exhibit no reducing properties. No ring closures have been attempted with (III).

The ethyl hydrogen esters (I) and (II) were readily cyclised by acetic anhydride–sodium acetate, the *cis*-ester giving *ethyl* 4-*acetoxy*-7-*phenylcoumarone*-6-*carboxylate* (IV; R = Ac, R′ = Et) and the *trans*-ester giving *ethyl* 1-*acetoxy*-4-(2′-*furyl*)*naphthalene*-3-*carboxylate* (V; R = Ac; R′ = Et).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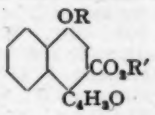
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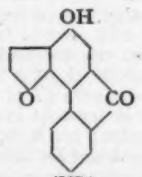
(VI.)

The identity of the ethyl hydrogen esters and their cyclisation products was shown by oxidation of (IV) and (V) with permanganate; the former gave an almost theoretical yield of benzoic acid, but the latter gave no identifiable product.

(IV) and (V) gave on mild hydrolysis *ethyl* 4-*hydroxy*-7-*phenylcoumarone*-6-*carboxylate* (IV; R = H, R′ = Et) and *ethyl* 1-*hydroxy*-4-(2′-*furyl*)*naphthalene*-3-*carboxylate* (V; R = H, R′ = Et) respectively. Further hydrolysis yielded 4-*hydroxy*-7-*phenylcoumarone*-6-*carboxylic acid* (IV; R = R′ = H) and 1-*hydroxy*-4-(2′-*furyl*)-*naphthalene*-3-*carboxylic acid* (V; R = R′ = H). The acids were characterised by their *acetyl* derivatives. Both (IV) and (V) (R = H) coupled normally with diazonium salts to give red dyes.

Further cyclisation of (IV; R = R′ = H) with concentrated sulphuric acid gave 2-*hydroxy*-9-*keto*-3′ : 2′ : 3 : 4-*furofluorene* (VI), purified and obtained crystalline through its *acetyl* derivative.

* Patent pending.

Alternatively (IV; R = Ac, R′ = H) was converted into its *acid chloride* and *anhydride* and cyclised by aluminium chloride, yielding the acetyl derivative of (VI).

The sodium salt of (VI) is distinguished by its deep purple colour, corresponding to the blue sodium salt of the hydroxybenzfluorenone of Borsche (*loc. cit.*). Various derivatives of (VI) were formed, including the acetate, the *benzoate*, and the *methyl ether*, and its *oxime*. (VI) functioned as a colour coupler in photographic developers, forming with the oxidation product of dialkyl-*p*-phenylenediamines a warm brown dye image (patent pending).

Attempts further to cyclise (V; R′ = H) gave no crystalline products.

From the *cis*-phenylfurylitaconic acid (I; R = H) a good yield of *1-keto-3-(2′-furyl)indene-2-acetic acid* was obtained on cyclisation with cold concentrated sulphuric acid. It was characterised by its 2 : 4-*dinitrophenylhydrazone*, and on refluxing with acetic anhydride–sodium acetate gave an excellent yield of the acetyl derivative of (VI).

The *trans*-phenylfurylitaconic acid could not be cyclised.

Experimental.

Analyses are by Drs. Weiler and Strauss, Oxford. M. p.'s are corrected. The majority of the compounds have a softening-melting range rather than a sharp m. p., even after repeated crystallisation.

Phenyl furyl ketone, prepared according to Marquis (*Ann. Chim. Phys.*, 1905, **4**, 276) from furoyl chloride, distilled at 285°/760 mm.

Ethyl Hydrogen cis-*γ-Phenyl-γ-(2-furyl)itaconate* (I; R = Et).—A mixture of phenyl furyl ketone (68·8 g.; 0·4 mol.) and ethyl succinate (66·7 c.c.; 0·4 mol.) was added in a thin stream, with shaking, to a warm solution of sodium ethoxide (18·4 g.; 0·8 mol. of sodium) in absolute alcohol; it turned red and partly gelled. The whole was heated on the water-bath for ½ hour, and water then added until no more oil was precipitated. The oil, consisting of neutral components, was removed in ether, and the alkaline solution acidified. The oil thus precipitated was dissolved in ether and dried (sodium sulphate), and the ether removed. The yellow-brown oil slowly formed a mass of oil-soaked crystals. These were separated from the oil (40 g.; not further examined) by filtration and washed with a little ether (yield, 40 g.; 33% of the theoretical). Recrystallised from aqueous acetone, they gave lustrous flat needles, m. p. 154—156° after softening at 149° (Found: C, 68·0; H, 5·4. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·4%). With concentrated sulphuric acid a blood-red solution was formed.

Ethyl Hydrogen trans-*γ-Phenyl-γ-(2-furyl)itaconate* (II; R = Et).—A mixture of phenyl furyl ketone (100 g.; 0·58 mol.) and ethyl succinate (95 c.c.; 0·58 mol.) was shaken at room temperature with a solution of sodium ethoxide (26·5 g.; 1·16 mols. of sodium) in an excess of absolute alcohol. After 12 hours, the whole was heated on the water-bath for 15 minutes, and water added. The precipitated neutral oil was removed in ether, and the alkaline solution neutralised with dilute hydrochloric acid. The oil thus precipitated solidified completely (yield, 109 g.). (If the alkaline solution was acidified, the oil only partly solidified, possibly owing to precipitation of an oily by-product by the excess of acid.) The cake was broken up, dried in a vacuum, and dissolved in methylene chloride, and ligroin gradually added. The first crop of crystals (10 g.) consisted of the ethyl hydrogen *cis*-ester, m. p. 154—156°, and the second crop (70 g.), m. p. 93—96°, of the *trans*-form (27·5%). Recrystallised from benzene–ligroin, the *ethyl hydrogen* trans-*ester* formed light fawn needle clusters, m. p. 93—96° (Found: C, 68·2; H, 5·4%). With concentrated sulphuric acid a blood-red solution was formed.

cis-*γ-Phenyl-γ-(2-furyl)itaconic Acid* (I; R = H).—A solution of the ethyl hydrogen *cis*-ester (5 g.) in 2·5% aqueous potassium hydroxide (200 c.c.) was boiled for 1 hour, acidified while hot, and allowed to cool. The crystals obtained were recrystallised from methanol–hot water, the cis-*acid* forming colourless prisms (4 g.), m. p. 208—215° (decomp.) (Found: C, 65·9; H, 4·5. $C_{15}H_{12}O_5$ requires C, 66·1; H, 4·5%).

trans-*γ-Phenyl-γ-(2-furyl)itaconic Acid* (II; R = H).—The ethyl hydrogen *trans*-ester was treated similarly. Acidification produced a yellow oil, which slowly crystallised. From benzene, the trans-*acid* formed fawn prisms (4·1 g.), m. p. 148—154° (Found: C, 66·4; H, 4·5%).

Reduction of cis- *and* trans-*Phenylfurylitaconic Acids: γ-Phenyl-γ-(2-furyl)pyroracemic Acids* (III).—10% Sodium amalgam (30 g.) was added during 6 hours to a solution of the acid (0·2 g.) in 10% aqueous sodium hydroxide (100 c.c.) heated on the water-bath, carbon dioxide being passed over the surface. The solution was decanted, the mercury washed, and the combined aqueous solutions filtered and acidified. From both acids, bulky white precipitates were obtained, which were washed with water and recrystallised from hot water.

The *pyroracemic acid* from the *cis*-itaconic acid formed balls of fine silky needles, m. p. 93—98°, and that from the *trans*-itaconic acid formed long silky needles, m. p. 103—108°. The mixed m. p. was never lower than 93—98°. Both acids contained one molecule of water of crystallisation (Found: for acid of m. p. 93—98°, C, 61·6; H, 5·5; for *acid* of m. p. 103—108°, C, 62·0; H, 5·6. $C_{14}H_{14}O_5,H_2O$ requires C, 61·6; H, 5·5%).

Ring Closures with Ethyl Hydrogen cis-*Phenylfurylitaconate* (I; R = Et).—(a) *With sulphuric acid.* The ester (0·5 g.) was dissolved in ice-cold concentrated sulphuric acid (10 c.c.), and the deep red solution kept at 4° for 20 hours and poured into water; red flocks formed which could not be crystallised. They gave a dirty brown dinitrophenylhydrazone, which also could not be obtained crystalline.

(b) *With acetic anhydride.* A mixture of the ester (61·0 g.), anhydrous sodium acetate (40 g.), and acetic anhydride (210 c.c.) was boiled for 3 hours, the yellow liquor concentrated in a vacuum, and the remaining anhydride decomposed with water. The yellow oil slowly crystallised. The yield of crude *ethyl 4-acetoxy-7-phenylcoumarone-6-carboxylate* (IV; R = Ac, R′ = Et) was almost theoretical. Recrystallised from methanol, it formed white crystal aggregates, m. p. 105—108°. It fluoresced blue in ultra-violet light (Found: C, 70·3; H, 4·9. $C_{19}H_{16}O_5$ requires C, 70·35; H, 5·0%).

Ethyl 4-hydroxy-7-phenylcoumarone-6-carboxylate (IV; R = H, R′ = Et) was readily obtained on acidification of the solution obtained by dissolving the acetoxy-derivative in spirit and adding an excess of warm 5% aqueous sodium hydroxide. From hot dilute acetic acid, it formed colourless needles, m. p. 178—181°; these absorbed ultra-violet light strongly (Found: C, 71·85; H, 5·1. $C_{17}H_{14}O_4$ requires C, 72·3; H, 5·0%).

4-Hydroxy-7-phenylcoumarone-6-carboxylic Acid (IV; R = R′ = H).—The crude acetoxy-ester (4·5 g.) was dissolved in spirit (10 c.c.) and boiled for 2 hours with 4% aqueous potassium hydroxide (50 c.c.). The solution was concentrated to half its volume in a vacuum, diluted to 100 c.c. with water, and acidified while hot. The yellow oil obtained soon solidified. From dilute acetic acid, it formed buff-coloured flat needles, m. p. 214—217°, containing ½ mol. of water of crystallisation, removable by heating above 110° for 3 hours (Found: C, 68·6; H, 4·15. $C_{15}H_{10}O_4,\frac{1}{2}H_2O$ requires C, 68·4; H, 4·2%). The red dye obtained by coupling with diazotised aniline formed red spears, m. p. 230—236° (decomp.), from chloroform.

4-Acetoxy-7-phenylcoumarone-6-carboxylic acid (IV; R = Ac, R′ = H) was formed on warming (IV; R = R′ = H) with acetic anhydride and sodium acetate for 5 minutes on the water-bath. It crystallised from methanol in colourless prisms which effloresced, releasing methanol of crystallisation. Dried at 100°/20 mm. for 2 hours, it formed a colourless powder, m. p. 236—238° (Found: C, 68·8; H, 4·15. $C_{17}H_{12}O_5$ requires C, 68·9; H, 4·1%).

Ring Closure of 4-Hydroxy-7-phenylcoumarone-6-carboxylic Acid.—The coumarone (5 g.) was dissolved in ice-cold concentrated sulphuric acid (100 c.c.) and after 15 minutes the green solution was poured into ice-water, and the flocculent brick-red precipitate collected and washed. The crude fluorenone could not be crystallised, so it was acetylated by solution in hot acetic anhydride and sodium acetate, giving, on recrystallisation from methanol, golden needles of *9-keto-2-acetoxy-3′ : 2′ : 3 : 4-furofluorene*, m. p. 169—171° (Found: C, 73·5; H, 3·7. $C_{17}H_{10}O_4$ requires C, 73·4; H, 3·6%). The *2 : 4-dinitrophenylhydrazone* formed orange needles, m. p. 278—280°, from chloroform (Found: N, 12·45. $C_{23}H_{14}O_7N_4$ requires N, 12·2%).

When an alcoholic solution of the acetoxy-derivative was warmed with an excess of sodium hydroxide, the yellow solution became deep purple. It was neutralised, and the red precipitate collected and crystallised from glacial acetic acid, forming blood-red plates, m. p. 221—227°, of *2-hydroxy-9-keto-3′ : 2′ : 3 : 4-furofluorene* (VI) (Found: C, 76·8; H, 3·7. $C_{15}H_{10}O_3$ requires C, 76·2; H, 3·4%). The sodium salt formed purple needles or spears.

Ring Closure of 4-Acetoxy-7-phenylcoumarone-6-carboxylic Acid: 9-Keto-2-acetoxy-3′ : 2′ : 3 : 4-furofluorene.—(a) *With aluminium chloride and the acid chloride.* The acetoxy-derivative (2 g.) was covered with thionyl chloride (10 c.c.) and warmed, hydrogen chloride being briskly evolved. The excess of thionyl chloride was distilled, and the residue, which soon solidified to a yellow crystalline cake, recrystallised from benzene. The *acid chloride* formed colourless needles, m. p. 157—160° (Found: Cl, 11·3. $C_{17}H_{11}O_4Cl$ requires Cl, 11·3%). It was dissolved in carbon disulphide (20 c.c.), aluminium chloride (2 g.) added, and the mixture warmed for 1 hour on the water-bath. The carbon disulphide was driven off, and the black residue decomposed with dilute hydrochloric acid. The yellow flocks (1·2 g.) crystallised from methanol in yellow needles, m. p. 169°, identical with the acetyl derivative of (VI) obtained from the sulphuric acid cyclisation product.

(b) *With aluminium chloride and the anhydride.* The acetylated acid (2 g.) and acetyl chloride (15 c.c.) were warmed until evolution of hydrogen chloride ceased; the excess of solvent was then removed in a vacuum, leaving an oil which soon crystallised. Recrystallised from benzene, the *anhydride* formed colourless plates, m. p. 110—114° (Found: C, 70·9; H, 3·8. $C_{34}H_{22}O_9$ requires C, 71·1; H, 3·9%). The crude anhydride, treated as in the case of the acid chloride, yielded the desired acetoxy-compound (1·3 g.), m. p. 170°.

The *benzoate* formed canary-yellow needles, m. p. 183—184°, from benzene (Found: C, 77·5; H, 3·5. $C_{22}H_{12}O_4$ requires C, 77·6; H, 3·6%). The *methyl ether* formed fine orange needles, m. p. 159—160°, from methanol (Found: C, 76·75; H, 4·1. $C_{16}H_{10}O_3$ requires C, 76·8; H, 4·0%), and its *oxime* canary-yellow needles, m. p. 233—234°, from methanol (Found: N, 5·25. $C_{16}H_{11}O_3N$ requires N, 5·3%).

Ring Closure of cis-γ-Phenyl-γ-(2-furyl)itaconic Acid (I; R = H).—(a) With acetic anhydride and sodium acetate a brown oil was obtained which could not be crystallised.

(b) *With sulphuric acid.* The *cis*-acid (0·54 g.), added slowly to concentrated sulphuric acid (15 c.c.) at 25°, dissolved to a deep green solution. After 15 minutes this was poured into ice-water, and the precipitate collected, washed with water, and recrystallised from acetic acid, giving brick-red needles (0·4 g.), m. p. 192—197°, of *1-keto-3-(2′-furyl)indene-2-acetic acid* (Found: C, 70·4; H, 4·0. $C_{15}H_{10}O_4$ requires C, 70·8; H, 4·0%). The *2 : 4-dinitrophenylhydrazone*, recrystallised from alcohol, had m. p. 215—217° (Found: N, 12·75. $C_{21}H_{14}O_7N_4$ requires N, 12·9%).

The indoneacetic acid (0·8 g.) was boiled for 1½ hours with acetic anhydride (5 c.c.) and anhydrous sodium acetate (0·5 g.). After destruction of the acetic anhydride 0·8 g. of 9-keto-2-acetoxy-3′ : 2′ : 3 : 4-furofluorene, m. p. 170°, was obtained.

Cyclisation of Ethyl Hydrogen trans-γ-Phenyl-γ-(2-furyl)itaconate: Ethyl 1-Acetoxy-4-(2′-furyl)naphthalene-3-carboxylate (V; R = Ac, R′ = Et).—The ethyl hydrogen *trans*-ester (61 g.), anhydrous sodium acetate (40 g.), and acetic anhydride (210 c.c.) were boiled for 3 hours, most of the anhydride removed in a vacuum, and the rest poured into water. The dark brown oil solidified. Recrystallised from *iso*propyl ether–ligroin or methanol, the *substance* formed fawn leaflets (55 g.), m. p. 78—81° (Found: C, 70·2; H, 4·9. $C_{19}H_{16}O_5$ requires C, 70·35; H, 5·0%).

Ethyl 1-hydroxy-4-(2′-furyl)naphthalene-3-carboxylate (V; R = H, R′ = Et) was readily formed by warming an alcoholic solution of the 1-acetoxy-derivative with 10% aqueous potassium hydroxide and acidifying the product. Recrystallised from dilute acetic acid, the substance formed fawn needles, m. p. 151—153° (Found: C, 71·9; H, 4·9. $C_{17}H_{14}O_4$ requires C, 72·3; H, 5·0%).

1-Hydroxy-4-(2′-furyl)naphthalene-3-carboxylic Acid (V; R = R′ = H).—The ethyl ester (5 g.), dissolved in spirit (25 c.c.), was boiled with 5% aqueous potassium hydroxide (100 c.c.) for 2 hours. After filtration and neutralisation the *acid* was recrystallised from methanol–hot water (Found: C, 70·6; H, 4·2. $C_{15}H_{10}O_4$ requires C, 70·8; H, 4·0%). It coupled with diazotised aniline, giving a red dye, reduced silver nitrate, and gave with concentrated sulphuric acid a red coloration.

1-Acetoxy-4-(2′-furyl)naphthalene-3-carboxylic acid (V; R = Ac, R′ = H), obtained on acetylating the above acid, recrystallised from acetone–ligroin in fine needles, m. p. 154—156° (Found: C, 68·65; H, 4·2. $C_{17}H_{12}O_5$ requires C, 68·9; H, 4·1%).

RESEARCH LABORATORIES, KODAK, LTD.,
WEALDSTONE, HARROW, MIDDLESEX.

[*Received, September 26th*, 1944.]

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49. *Transport Numbers of Zinc Halides.*

By (MISS) D. M. EGAN and J. R. PARTINGTON.

The transport numbers of zinc chloride, bromide, and iodide, over the following ranges of molar concentration: zinc chloride 0·01—0·33, zinc bromide 0·01—0·33, zinc iodide 0·01—0·21, have been measured by the Hittorf method. The results indicate that zinc chloride behaves as a typical 2, 1 type electrolyte over the range of molarity studied and there is no indication of the presence of complex ions. Zinc bromide behaves similarly up to 0·25M., but at higher concentrations there are indications of the presence of small quantities of complex ions. Zinc iodide has an abnormally low cation transport number even at low concentrations, and the rapid decrease of cation transport number with increase of concentration suggests that a complex ion, such as ZnI_3^-, is present.

In a previous research (J., 1943, 157) it was found that the activity coefficients of zinc iodide are those of a typical 2, 1 type electrolyte up to 0·05M., but at higher concentrations they increase rapidly with concentration. This suggests that complex ions are present in the more concentrated solutions. Further evidence of the presence of complex ions could be obtained from transport number measurements. Although much information is available for cadmium salts, few determinations of transport numbers have been made with zinc halides (Hittorf, *Ann. Physik*, 1859, **106**, 513; *Z. physikal. Chem.*, 1901, **39**, 613; 1903, **43**, 239; Bein, *Ann. Physik*, 1892, **46**, 29; *Z. physikal. Chem.*, 1898, **27**, 1; 1899, **28**, 439; Kümmell, *Ann. Physik*, 1898, **64**, 655; Drucker, *Z. Elektrochem.*, 1913, **19**, 797). The present paper deals with the transport numbers of zinc chloride, bromide, and iodide as determined by the Hittorf method.

Experimental.

Solutions.—Zinc chloride, bromide, and iodide solutions were prepared as previously described (J., 1943, 159). The zinc and halogen contents of all newly prepared solutions were determined gravimetrically; in subsequent experiments only the halogen was determined, except in concentrated solutions, for which both the zinc and the halogen contents were determined to confirm the absence of basic salt. In the analyses 10, 20, or 40 ml. of solution (according to the concentration) were weighed, and the halogen content determined as silver halide. Corresponding analyses agreed to within 0·0004 g. of silver halide.

Electrodes.—The anode, which was of the same pure (99·99%) zinc as was previously used, was in the form of a rod, 3·5 cm. long and 0·7 cm. in diameter, fitted with sealing wax into a glass tube which was filled with mercury; contact with the external circuit was made by a copper wire dipping into the mercury. With fairly dilute solutions unamalgamated zinc was satisfactory, but above 0·1M. a white deposit of basic salt was formed. In order to prevent this, the zinc electrodes were amalgamated by placing them in mercurous nitrate solutions containing 5% of nitric acid for half an hour. All solutions were kept air-free by storage in completely filled stoppered bottles. No deposit formed on the amalgamated electrodes within the concentration range studied, and they were used throughout this research.

Pure mercury was used as the cathode. In dilute solutions (below 0·1M.), the zinc was deposited on the mercury in a sparingly soluble form, whilst that from more concentrated solutions was much more soluble. A similar phenomenon was noticed by Hittorf (*loc. cit.*) with cadmium salts.

Cells.—The electrolytic cell was a slight modification of that described by Findlay (*Chem. News*, 1909, **100**, 185; "Practical Physical Chemistry," 1941, p. 189). It consisted of similar anode and cathode compartments joined to a central U-tube (middle compartment) by rubber tubing. Each limb had a bulb at the lower end to reduce the resistance, and the anode and middle compartments each had an exit tube at the bottom, fitted with rubber tubing and a screw clip. The open end of this rubber tubing was closed by a piece of glass rod to prevent ingress of water from the thermostat. The cathode compartment was without an exit tube at the bottom. This form of the apparatus can be used in a water thermostat, and so has an advantage over one with glass stopcocks. The side arms and U-tube were 1·8 cm. in diameter, and were joined by pieces of soft black rubber tubing, which was previously boiled in distilled water for 15 minutes. If the side arms or rubber tubing are too narrow, heating occurs at these points owing to the increased resistance.

Current from the mains (220 or 110 volts) was passed through a suitable resistance.

Coulometer.—The quantity of electricity passing was measured by a silver coulometer. The cathode of this consisted of a platinum dish of 80 ml. capacity, cleaned with nitric acid, washed with water, and dried at 140°. The anode was a thick wire of pure silver, wound in a horizontal coil, and enclosed in a bag of filter-paper secured by sewing-cotton which had been boiled for some time in distilled water. The function of the filter paper is to retain the anode slime. The use of filter-paper was recommended by Rayleigh and Sidgwick (*Phil. Trans.*, 1884, **175**, 411), but disapproved by Richards, Collins, and Heimrod (*Z. physikal. Chem.*, 1900, **32**, 321), who used a small porous pot. The influence of good, unsized paper on the results is probably quite negligible. Pure silver nitrate was recrystallised from a solution slightly acidified with nitric acid, and a 15% solution was stored in a dark bottle. The platinum dish stood on a glass plate, and the coulometer was enclosed in a box to exclude light during the experiment. After the experiment the dish with the silver deposit was washed with distilled water, filled with water and left overnight, and finally rinsed with alcohol and dried at 140°.

Experimental Procedure.—The silver coulometer and a milliammeter (to give an approximate measure of the current strength) were joined in series with the cell. The thermostat stirrer must operate rather slowly so as not to cause vibration of the transport apparatus. All measurements were made at 25°. The cell was filled with zinc halide solution of known concentration, and a current of 0·01—0·04 amp. was passed through the circuit for 1½–3 hours, the current strength and duration of the experiment depending on the concentration of the solution. If the current strength is too high, heating and convection currents are produced, causing mixing in the solution, and if the experiment is continued too long the middle solution will have changed in composition. At the end of the experiment the screw clips on the U-tube rubber were closed, the apparatus removed from the thermostat, and the liquid in the anode compartment run into a weighed flask; the compartment was rinsed with some of the original solution, and the total amount of liquid weighed and analysed. The solution in the middle compartment was withdrawn and analysed, and if it had changed in composition the experiment was rejected. In several cases the cathode solution was also analysed, but this did not give satisfactory results, probably owing to the difficulty of washing the mercury and zinc deposit to remove all the solution.

Experimental Results.—The cation transport number is given by

$$n_c = \frac{\text{No. of equivalents of zinc lost from anode compartment}}{\text{No. of equivalents of silver deposited in coulometer}}$$

The analyses of the solutions are given in Tables I, III, and V. Col. 1 gives the molarity of the solution, cols. 3 and 2 the weight of silver halide produced from x g. of zinc halide solution before the experiment, and col. 4 the weight of zinc associated with 1 g. of water. Cols. 5, 6, and 7 give similar analytical data for the anode solution after electrolysis, and 8 and 9 the middle solution analyses. Details of the experiments, and the transport numbers obtained, are given in Tables II, IV, and VI, in which col. 1 gives the molarity, cols. 2 and 3 the mean current strength and the duration of the experiment (in minutes), respectively, 4 the weight of silver deposited in the coulometer, 5 the weight of the anode solution, and 6 and 7 the zinc contents of the anode solution before and after electrolysis, respectively. The cation transport number is given in the last column, and a graph of n_c against molarity is given in the figure.

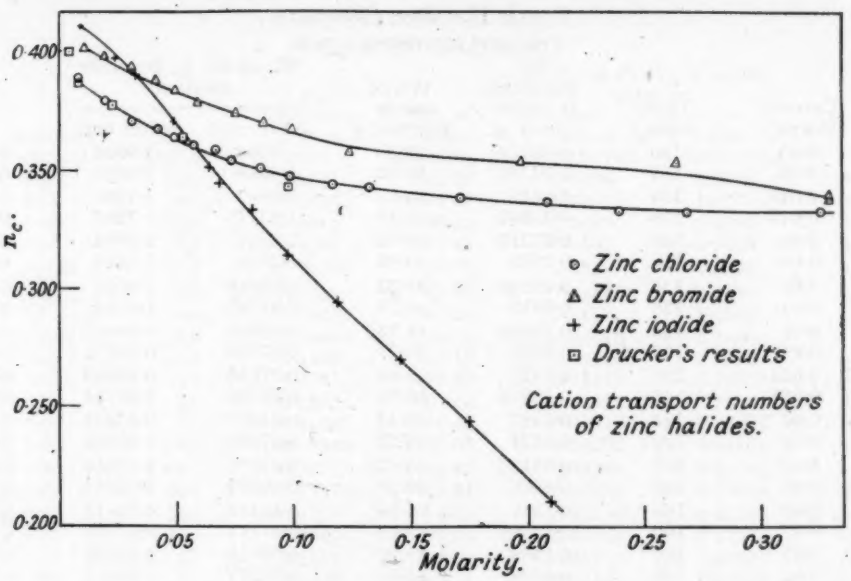


TABLE I.

Zinc Chloride.

Analyses of solutions.

	Anode solution before expt.			Anode solution after expt.			Middle solution.	
Molarity.	Weight of AgCl from x g. of solution. x.	AgCl.	Wt. of Zn ≡ 1 g. of H_2O.	Weight of AgCl from x g. of solution. x.	AgCl.	Wt. of Zn ≡ 1 g. of H_2O.	Weight of AgCl from x g. of solution. x.	AgCl.
0·3271	20·74	1·8753	0·021545	10·40	0·9870	0·022667	10·38	0·9379
				10·39	0·9875	0·022697	10·37	0·9375
0·2800	20·62	1·6056	0·18463	10·33	0·8389	0·019264	10·32	0·8033
				10·33	0·8389	0·019264	10·31	0·8027
0·2102	20·46	1·2052	0·013817	10·24	0·62875	0·14424	10·23	0·6030
				10·25	0·6310	0·14459	10·22	0·6021
0·1724	20·35	0·9886	0·011340	20·37	1·0403	0·011938	20·36	0·9889
				20·36	1·0390	0·011928	20·35	0·9880
0·1500	20·29	0·86025	0·0098682	20·30	0·90305	0·010364	20·28	0·8607
				20·31	0·9000	0·010323	20·28	0·86025
0·1344	20·26	0·77065	0·0088359	20·27	0·8089	0·0092797	20·27	0·7704
				20·27	0·80915	0·0092797	20·26	0·7709
0·0986	20·18	0·5654	0·0064764	20·22	0·59665	0·0068256	20·17	0·5658
				20·23	0·59655	0·0068203	20·18	0·5651
0·0862	20·15	0·4943	0·0056590	20·18	0·5218	0·0059707	20·16	0·4950
				20·19	0·5214	0·0059634	20·16	0·4950
0·0750	20·125	0·4300	0·0049229	20·17	0·4568	0·0052211	20·13	0·4304
				20·16	0·4582	0·0052400	20·14	0·4296
0·0672	20·104	0·3853	0·0044088	20·15	0·4103	0·0046903	20·12	0·3849
				20·14	0·4115	0·0047599	20·11	0·3852
0·0581	20·07	0·3332	0·0038167	20·13	0·3590	0·0041020	20·09	0·3336
				20·125	0·35965	0·0041105	20·08	0·3329
0·0500	20·06	0·2867	0·0032817	20·16	0·31225	0·0035585	20·11	0·2865
				20·155	0·3121	0·0035578	20·14	0·2872
0·0431	20·05	0·24715	0·0028282	20·14	0·27045	0·0030819	20·05	0·2469
				20·14	0·2719	0·0030987	20·045	0·2470
0·0327	20·02	0·1876	0·0021467	20·10	0·2073	0·0023637	20·03	0·1877
				20·09	0·20835	0·0023772	20·03	0·1881
0·0210	39·98	0·24085	0·0013777	40·02	0·27445	0·0015692	39·99	0·2406
				40·03	0·27225	0·0015562	40·00	0·2410
0·0097	39·92	0·11065	0·0006328	40·01	0·13862	0·0007914	39·92	0·1108
				39·99	0·14065	0·0008030	39·92	0·1105

TABLE II.—*Zinc Chloride.*

Transport experiment results.

Molarity.	Current (amps.).	Time (mins.).	Ag deposited in coulometer, g.	Wt. of anode solution, g.	Wt. of Zn, g., in anode solution, before expt.	Wt. of Zn, g., in anode solution, after expt.	n_z.	
0·3271	0·05	150	0·50115	92·38	1·9004	1·9995	0·3222	0·333
	0·05	155	0·51760	95·02	1·9548	2·0593	0·3337	
0·2800	0·045	120	0·3621	95·02	1·6867	1·7597	0·3348	0·333
	0·045	120	0·35445	93·39	1·6577	1·7295	0·3315	
0·2102	0·04	105	0·27215	92·72	1·2437	1·2984	0·3368	0·337
	0·04	115	0·2805	89·86	1·2053	1·2616	0·3376	
0·1724	0·03	125	0·25165	86·33	0·95519	1·0055	0·3392	0·338
	0·03	130	0·2519	86·33	0·97742	1·0281	0·3360	
0·1500	0·03	105	0·21035	86·755	0·83802	0·88016	0·3389	0·341
	0·03	105	0·2029	90·79	0·87708	0·91751	0·3423	
0·1344	0·025	110	0·1927	88·89	0·77050	0·80903	0·3417	0·342
	0·025	110	0·19385	88·70	0·76890	0·80754	0·3422	
0·0986	0·02	115	0·1487	85·41	0·54537	0·57478	0·3473	0·347
	0·02	120	0·1521	89·35	0·57056	0·60088	0·3462	
0·0862	0·02	105	0·13425	85·835	0·47975	0·50618	0·3503	0·351
	0·02	105	0·1368	89·32	0·49922	0·52609	0·3518	
0·0750	0·02	105	0·1347	89·28	0·43479	0·46114	0·3545	0·355
	0·02	100	0·13555	84·42	0·41111	0·43759	0·3560	
0·0672	0·02	100	0·1308	90·99	0·39728	0·42264	0·3601	0·361
	0·02	100	0·1298	85·50	0·37331	0·39842	0·3616	
0·0581	0·015	135	0·1279	86·94	0·32899	0·35359	0·3653	0·363
	0·015	135	0·12855	85·27	0·32269	0·34756	0·3616	
0·0500	0·02	100	0·1225	85·93	0·27993	0·30353	0·3641	0·365
	0·02	100	0·1297	90·90	0·29611	0·32102	0·3662	
0·0431	0·015	120	0·1178	89·50	0·25151	0·27407	0·3680	0·369
	0·015	120	0·1193	84·76	0·23817	0·26098	0·3691	
0·0327	0·015	100	0·10155	89·54	0·19127	0·21060	0·3718	0·372
	0·015	105	0·1047	86·78	0·18536	0·20528	0·3722	
0·0210	0·01	135	0·0899	88·54	0·12159	0·13847	0·3804	0·379
	0·01	135	0·09125	85·65	0·11763	0·13285	0·3772	
0·0097	0·015	80	0·0791	92·26	0·058290	0·072895	0·3907	0·390
	0·010	105	0·0823	89·48	0·056532	0·071767	0·3891	

TABLE III.—*Zinc Bromide.*

Analyses of solutions.

	Anode solution before expt.			Anode solution after expt.			Middle solution.	
Molarity.	Weight of AgBr from x g. of solution. x.	AgBr.	Wt. of Zn ≡ 1 g. of H_2O.	Weight of AgBr from x g. of solution. x.	AgBr.	Wt. of Zn ≡ 1 g. of H_2O.	Weight of AgBr from x of solution. x.	AgBr.
0·3291	10·64	1·2359	0·021727	10·66	1·2771	0·022468	10·64	1·23585
				10·645	1·2702	0·022390	10·635	1·2360
0·3268	10·62	1·2272	0·021611	10·66	1·2901	0·022718	10·615	1·2266
				10·665	1·3017	0·022924	10·62	1·2278
0·2650	10·51	0·9950	0·017454	10·53	1·0377	0·018234	10·51	0·9945
0·1984	10·38	0·7446	0·013049	10·39	0·7806	0·013690	10·39	0·7446
				10·415	0·8003	0·014022	10·39	0·7450
0·1251	10·245	0·4689	0·0081919	10·245	0·4955	0·0086702	10·23	0·4689
				10·25	0·4940	0·0087226	10·24	0·4687
				10·235	0·4928	0·0086137	10·23	0·4683
0·1016	20·33	0·7628	0·0066823	20·34	0·8313	0·0072932	10·17	0·3812
				20·36	0·7904	0·0069193	10·17	0·3814
				20·33	0·7930	0·0069522	10·165	0·3814
0·0872	20·225	0·6552	0·0057120	20·25	0·6968	0·0061174	20·23	0·6558
				20·25	0·6918	0·0060716	20·23	0·6552
0·0760	10·12	0·2855	0·0049945	20·24	0·6020	0·0052715	20·23	0·5714
				20·22	0·6054	0·0053068	20·22	0·5713
0·0601	20·11	0·4513	0·0039595	20·16	0·4795	0·0042005	20·12	0·4513
				20·14	0·4812	0·0042195	20·12	0·4513
0·0499	20·13	0·3749	0·0032786	20·13	0·3987	0·0034893	20·13	0·3747
				20·13	0·4071	0·0035555	20·12	0·3754
0·0410	20·07	0·3081	0·0026969	20·09	0·3311	0·0028977	20·07	0·30825
				20·08	0·3343	0·0029277	20·06	0·3070
0·0310	20·04	0·2326	0·0020342	20·06	0·2543	0·0022238	20·04	0·2330
				20·06	0·2532	0·0022139	20·05	0·2328
0·0201	40·02	0·3011	0·0013186	40·06	0·3408	0·0014884	20·00	0·1506
				40·00	0·3345	0·0014303	20·00	0·1507
0·0119	19·97	0·0891	0·0007786	19·96	0·1005	0·0008790	19·96	0·0890
				19·93	0·0969	0·0008488	19·96	0·0887

TABLE IV.—*Zinc Bromide.*

Transport experiment results.

Molarity.	Current (amps.).	Time (mins.).	Ag deposited in coulometer, g.	Wt. of anode solution, g.	Wt. of Zn, g., in anode solution, before electrolysis.	Wt. of Zn, g., in anode solution, after electrolysis.	n_e.	
0·3291	0·03	160	0·3191	92·62	1·8679	1·9315	0·3422	0·341
	0·03	140	0·28955	94·17	1·8996	1·9575	0·3401	
0·3268	0·05	150	0·4974	96·81	1·9402	2·0395	0·3412	0·339
	0·05	150	0·4986	82·41	1·6507	1·7508	0·3375	
0·2650	0·035	145	0·34375	91·75	1·5068	1·5741	0·3539	0·354
0·1984	0·025	150	0·2618	83·02	1·0346	1·0856	0·3571	0·356
	0·04	143	0·38575	81·36	1·0127	1·0882	0·3541	
0·1251	0·022	135	0·19885	83·15	0·66142	0·70003	0·3593	0·358
	0·022	130	0·1896	85·17	0·67756	0·71453	0·3565	
	0·022	125	0·1881	89·43	0·71146	0·74809	0·3573	
0·1016	0·04	95	0·2542	81·95	0·53417	0·58301	0·3675	0·368
	0·02	90	0·11665	94·49	0·62973	0·65206	0·3682	
	0·02	95	0·12385	90·03	0·58750	0·61126	0·3669	
0·0872	0·025	100	0·1612	85·87	0·48368	0·51448	0·3694	0·371
	0·02	100	0·13475	81·84	0·46101	0·48669	0·3716	
0·0760	0·02	100	0·1299	90·38	0·44336	0·46795	0·3754	0·375
	0·02	100	0·13655	84·33	0·41366	0·43951	0·3753	
0·0601	0·02	85	0·1137	90·33	0·35255	0·37401	0·3772	0·377
	0·02	85	0·1130	83·14	0·32448	0·34580	0·3774	
0·0499	0·015	95	0·0950	84·98	0·27529	0·29299	0·3851	0·384
	0·02	100	0·1348	89·57	0·29008	0·31530	0·3826	
0·0410	0·017	80	0·0887	82·80	0·22109	0·23757	0·3868	0·388
	0·017	90	0·10185	82·63	0·22061	0·23948	0·3886	
0·0310	0·018	75	0·0897	87·46	0·17658	0·19300	0·3959	0·393
	0·015	80	0·0783	81·06	0·16368	0·17811	0·3919	
0·0201	0·015	85	0·08625	93·365	0·12248	0·13826	0·3963	0·398
	0·015	55	0·0543	86·85	0·11656	0·12646	0·3988	
0·0119	0·01	65	0·04425	80·05	0·06214	0·07015	0·4026	0·402
	0·01	45	0·03095	82·32	0·06236	0·06998	0·4010	

TABLE V.—*Zinc Iodide.*

Analyses of solutions.

	Anode solution before expt.			Anode solution after expt.			Middle solution.	
	Weight of AgI from x g. of solution.		Wt. of Zn ≡ 1 g. of H_2O.	Weight of AgI from x g. of solution.		Wt. of Zn ≡ 1 g. of H_2O.	Weight of AgI from x g. of solution.	
Molarity.	x.	AgI.		x.	AgI.		x.	AgI.
0·2106	10·61	0·9889	0·014230	10·67	1·0732	0·0150310	10·615	0·9893
				10·665	1·0701	0·0149920	10·61	0·9887
0·1768	10·515	0·8302	0·0116130	10·54	0·88165	0·0123480	10·52	0·8306
				10·54	0·8801	0·0123260	10·515	0·8303
0·1467	10·42	0·6889	0·0096374	10·44	0·73465	0·0102890	10·42	0·6892
				10·445	0·7359	0·0103020	10·415	0·6888
0·1197	10·31	0·5620	0·0078819	10·35	0·60905	0·0085342	10·305	0·5617
				10·355	0·6121	0·0085740	10·31	0·5621
0·1020	10·265	0·4790	0·0067098	10·29	0·5163	0·0072324	10·27	0·4792
0·0998	10·259	0·4687	0·0065648	10·27	0·4917	0·0068902	10·26	0·4685
				10·27	0·5019	0·0070361	10·255	0·46855
0·0961	10·245	0·4513	0·0063225	10·27	0·4840	0·0067788	10·25	0·4519
0·0880	10·225	0·4134	0·005703	10·24	0·4422	0·0061940	10·22	0·4131
0·0831	10·22	0·3901	0·0054584	10·24	0·4370	0·0061185	10·225	0·3900
				10·24	0·4361	0·0061058	10·22	0·3896
0·0728	10·18	0·3417	0·0047809	10·20	0·3674	0·0051405	10·18	0·3421
0·0702	10·175	0·3294	0·0046089	10·19	0·3551	0·0049700	10·17	0·3291
				10·19	0·3544	0·0049601	10·18	0·3298
0·0648	10·17	0·3045	0·0042564	10·18	0·3299	0·0046140	10·17	0·30445
				10·18	0·3337	0·0050016	10·165	0·3047
0·0503	20·20	0·4724	0·0033081	20·225	0·5051	0·0035371	20·21	0·4726
				20·22	0·50965	0·0035704	20·20	0·4729
0·0397	10·094	0·1863	0·0026285	10·10	0·1999	0·0027932	10·09	0·1859
0·0331	20·10	0·3104	0·0021726	20·10	0·3352	0·0023482	20·09	0·3098
				20·12	0·33945	0·0023718	20·09	0·3105
0·0256	10·061	0·1205	0·0016808	10·075	0·1324	0·0018463	10·06	0·12055
0·0256	20·05	0·2405	0·0016833	20·075	0·2605	0·0018220	20·05	0·24115
				20·075	0·2615	0·0018298	20·10	0·2403
0·0109	20·00	0·1021	0·0007132	20·015	0·1143	0·0007981	20·00	0·1017
				20·015	0·1148	0·0008017	20·05	0·1020

TABLE VI.

Zinc Iodide.

Transport experiment results.

Molarity.	Current (amps.).	Time (mins.).	Ag deposited in coulometer, g.	Wt. of anode solution, g.	Wt. of Zn, g., in anode solution, before electrolysis.	Wt. of Zn, g., in anode solution, after electrolysis.	n_c.	
0·2106	0·04	115	0·2785	89·36	1·1846	1·2514	0·2084	0·210
	0·04	105	0·2539	85·50	1·1337	1·1944	0·2110	
0·1768	0·04	105	0·2680	88·67	0·97120	1·0327	0·2427	0·244
	0·04	100	0·24045	81·72	0·89513	0·95007	0·2459	
0·1467	0·03	125	0·2377	84·775	0·77794	0·83048	0·2727	0·271
	0·03	125	0·23305	81·57	0·74841	0·80006	0·2686	
0·1197	0·03	125	0·2436	83·45	0·63142	0·68366	0·2925	0·294
	0·03	130	0·2537	81·57	0·61708	0·67125	0·2954	
0·1020	0·025	130	0·2132	88·22	0·57174	0·61626	0·3123	
0·0998	0·028	85	0·1569	103·20	0·65542	0·68791	0·3166	0·315
	0·028	115	0·1874	85·21	0·54080	0·57975	0·3140	
0·0961	0·03	90	0·1768	82·56	0·50523	0·5417	0·3192	0·323
0·0880	0·025	110	0·1839	95·70	0·53786	0·57536	0·3271	
0·0831	0·026	170	0·2664	84·23	0·44643	0·50043	0·3311	0·330
	0·026	160	0·2443	79·075	0·41915	0·46887	0·3284	
0·0728	0·02	115	0·1491	85·49	0·39875	0·42873	0·3365	
0·0702	0·025	95	0·15655	88·10	0·39641	0·42748	0·3449	0·344
	0·025	95	0·15960	92·765	0·41744	0·44925	0·3423	
0·0648	0·020	110	0·1435	80·85	0·33656	0·36482	0·3492	0·351
	0·022	115	0·1660	80·85	0·3347	0·36900	0·3533	
0·0503	0·022	75	0·10435	88·25	0·28698	0·30685	0·3716	0·371
	0·02	90	0·11455	84·92	0·27611	0·2980	0·3697	
0·0397	0·02	75	0·0835	96·54	0·25034	0·26603	0·3799	
0·0331	0·017	75	0·08085	85·82	0·18435	0·19925	0·3919	0·391
	0·02	70	0·0940	86·31	0·18536	0·20274	0·3902	
0·0256	0·01	110	0·0738	81·99	0·13659	0·15003	0·3990	
0·0256	0·016	65	0·0682	88·96	0·14842	0·16072	0·3956	0·397
	0·016	65	0·0673	84·43	0·14086	0·15313	0·3983	
0·0109	0·01	60	0·0401	84·55	0·060065	0·067217	0·4114	0·412
	0·01	60	0·0423	85·43	0·060695	0·068228	0·4123	

DISCUSSION OF RESULTS.

The curves n_c–M for zinc chloride and bromide resemble those for calcium chloride (Longsworth, *J. Amer. Chem. Soc.*, 1934, **57**, 1185; cf. Drucker and Luft, *Z. physikal. Chem.*, 1926, **121**, 307), barium chloride (Jones and Dole, *J. Amer. Chem. Soc.*, 1929, **51**, 1073), and cadmium chloride (Jahn, *Z. physikal. Chem.*, 1901, **37**, 673). The cation transport number of the chloride from 0·01 to 0·1M. decreases; after 0·1M. the decrease is very small. The cation transport number of the bromide begins to decrease rather more rapidly at about 0·25M., and it is possible that complex ions are present in these concentrated solutions. In the case of zinc chloride up to 0·33M., and zinc bromide up to 0·25M., there is no indication of the presence of complex ions. The results for the chloride agree well with those of Drucker (*loc. cit.*). The cation transport number of zinc iodide, on the contrary, varies considerably with concentration, and the n_c–M curve resembles that for cadmium iodide (Jahn, *loc. cit.*). This result was expected from the activity coefficients reported in the previous paper, and indicates that complex ions are present in solutions of quite low concentration, probably down to 0·03M. The marked fall in cation transport number with increasing concentration indicates the formation of complex anions and a negative value may ultimately be reached. Hittorf (*loc. cit.*) found that the cation transport numbers in concentrated zinc and cadmium iodide solutions were negative, and concluded that complex ions $(ZnI_4)^{--}$, $(CdI_4)^{--}$, respectively, are present. Jahn (*loc. cit.*) found similar results with cadmium iodide. McBain (*Z. Elektrochem.*, 1905, **11**, 215) correlated the transport, conductivity, and freezing-point data of previous workers for cadmium iodide, and concluded that a complex anion, probably $(CdI_3)^-$, is present, except in rather dilute solutions. Later (*J. Physical Chem.*, 1931, **34**, 999), McBain made transport measurements with cadmium chloride, bromide, and iodide, and in the last case attempted to calculate the amounts of the various possible ions present.

In this research the cation transport numbers of zinc iodide show a marked decrease with increase of concentration, and this, when correlated with the E.M.F. results, makes probable the existence of $(ZnI_3)^-$ or $(ZnI_4)^{--}$, or perhaps both, but it is a matter of difficulty to distinguish between the two. Bates and Vosburgh (*J. Amer. Chem. Soc.*, 1938, **60**, 137) concluded from E.M.F. measurements with cadmium iodide that the complex anion is $(CdI_3)^-$, and McBain (*loc. cit.*) considered that $(CdI_3)^-$ is much more likely than $(CdI_4)^{--}$, since the latter would be a large ion which would have a correspondingly low velocity, and would not readily

account for the observed conductivity and transference data. It seems probable that the complex anion in the case of zinc iodide is also $(ZnI_3)^-$, though the possibility of $(ZnI_4)^{--}$ cannot be ruled out.

The authors gratefully acknowledge the facilities kindly put at their disposal by Prof. R. G. W. Norrish, F.R.S., and the University of Cambridge, enabling them to carry out their work in the Cambridge laboratories.

QUEEN MARY COLLEGE (UNIVERSITY OF LONDON). [*Received, December 13th*, 1944.]

50. *Photo-reactions. Part IX. The Action of Aldehydes on Phenanthraquinoneimine in Sunlight.*

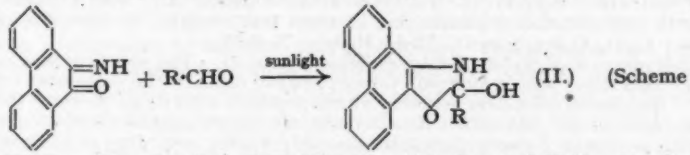
By ALEXANDER SCHÖNBERG and WILLIAM IBRAHIM AWAD.

In sunlight, aldehydes react with phenanthraquinoneimine with formation of 2-hydroxy-2 : 3-dihydrophenanthroxazole derivatives (see A). These decompose with loss of water on heating. There is a similarity between reaction (A) and the photo-reaction between phenanthraquinone and aldehydes which leads to substances of the general formula (III) (*e.g.*, R = Ph). The possibility of ring-chain tautomerism (II)⇄(IV) is discussed.

STEIN and DAY (*J. Amer. Chem. Soc.*, 1942, **64**, 2567) found that phenanthraquinoneimine (I) and benzaldehyde do not react when refluxed in alcohol, but in presence of a catalyst, *e.g.*, piperidine or triethylamine, reaction occurs with elimination of water and formation of 2-phenylphenanthroxazole :

$$(I) + Ph{\cdot}CHO \longrightarrow H_2O + C_{21}H_{13}ON$$

We have found that phenanthraquinoneimine does not react (or only to a very small extent) with benzaldehyde in benzene solution at room temperature in the dark, but in sunlight 2-hydroxy-2-phenyl-2 : 3-dihydrophenanthroxazole (II*b*) is formed. Similar reactions were carried out with acetaldehyde, *p*-anisaldehyde, *p*-chlorobenzaldehyde, piperonal, and 2-methoxy-1-naphthaldehyde. Reaction proceeds very rapidly with acetaldehyde, benzaldehyde, and *p*-anisaldehyde, but is considerably slower with 2-methoxy-1-naphthaldehyde, possibly owing to steric hindrance (ortho-effect).



[II*a*, R = Me. II*b*, R = Ph. II*c*, R = $C_6H_4{\cdot}OMe$ (*p*). II*d*, R = *p*-C_6H_4Cl. II*e*, R = $C_6H_3{\cdot}O_2CH_2$. II*f*, R = 2-OMe-1-$C_{10}H_6$]

Properties of the Photo-products.—The photo-products (II) are colourless or almost colourless crystalline substances of high m. p. They give colour reactions with concentrated sulphuric acid and are insoluble in cold aqueous sodium hydroxide. On oxidation with chromium trioxide phenanthraquinone is formed. They are also attacked when heated with precipitated selenium in a stream of air; from (II*b*), benzoic acid is thus formed. When heated, they decompose with loss of water and formation of the corresponding phenanthroxazole; (II*b*), *e.g.*, gives 2-phenylphenanthroxazole.

Constitution of the Photo-products. Possibility of Ring-chain Tautomerism.—The constitution of the photo-products is based on their insolubility in cold alkali and on their similarity with the products (III) formed when phenanthraquinone reacts with aldehydes in sunlight (Schönberg and Moubacher, J., 1939, 1430).

That the photo-products do not react vigorously with diazomethane is also in favour of the cyclic formula (II). There seems to be a strong tendency for 9 : 10-derivatives of phenanthrene to form rings; *e.g.*, phenanthrene-9 : 10-dicarboxylic acid is unstable and readily changes into the anhydride (Jeanes and Adams, *J. Amer. Chem. Soc.*, 1937, **59**, 2612). It is possible that in solution the substances show ring-chain tautomerism, (II)⇄(IV).

The substances (II*a*) and (II*b*) have been prepared by Pschorr (*Ber.*, 1902, **35**, 2733) and Auwers (*Annalen*, 1911, **378**, 216), respectively, who gave them formula (IV, R = Me or Ph).

EXPERIMENTAL.

General Remarks.—The photo-chemical reactions were carried out in a Monax glass tube, the air being displaced by dry carbon dioxide, and the tube sealed by fusion.* The benzene was thiophen-free and dried over sodium.

* The experiments of Schönberg and Mustafa (J., 1944, 67) also were carried out in Monax glass tubes, a fact not stated in the original paper.

Photo-chemical Reaction between Aldehydes and Phenanthraquinoneimine (I).—*Acetaldehyde.* The imine (1 g.) and acetaldehyde (10 g.) in benzene were exposed to sunlight for 11 days (August), the benzene then evaporated in a vacuum, and the residue washed with a small amount of benzene. It separated from benzene in colourless crystals, m. p. about 217° (red-brown melt), of 2-hydroxy-2-methyl-2 : 3-dihydrophenanthroxazole (II*a*), difficultly soluble in cold alcohol; it was soluble in concentrated sulphuric acid and boiling aqueous sodium hydroxide, giving orange solutions. The photo-product did not depress the m. p. of the substance described as 9-acetylamino-10-hydroxyphenanthrene by Pschorr (*loc. cit.*) (Found: C, 76·1; H, 5·4; N, 5·4. Calc. for $C_{16}H_{13}O_2N$: C, 76·5; H, 5·2; N, 5·6%).

Benzaldehyde. The experiment was carried out, as described above, with 0·5 g. of the imine and 2 g. of freshly distilled benzaldehyde in benzene (30 c.c.). After 3 hours, the colourless or slightly yellow crystals were collected, washed with benzene, and recrystallised from benzene, giving an almost quantitative yield of colourless 2-hydroxy-2-phenyl-2 : 3-dihydrophenanthroxazole (II*b*), m. p. about 236° (decomp.; red-brown melt), insoluble in dilute and in concentrated hydrochloric acid, difficultly soluble in hot benzene, soluble in boiling alcohol, and soluble in hot aqueous sodium hydroxide, giving a reddish-brown solution. It did not depress the m. p. of the product described as 9-benzoylamino-10-hydroxyphenanthrene by Auwers (*loc. cit.*), but in its preparation we avoided (in contrast to Auwers) the crystallisation from acetic acid (which seems to affect the substances) and crystallised it only from benzene (Found: C, 80·7; H, 5·0. Calc. for $C_{21}H_{15}O_2N$: C, 80·5: H, 4·8%).

p-*Anisaldehyde.* The imine (1 g.) and *p*-anisaldehyde (4 g.), dissolved in benzene (50 c.c.), were exposed for 1 day (August). The colourless crystals obtained were purified as described in the preceding experiment, giving 2-*hydroxy*-2-p-*anisyl*-2 : 3-*dihydrophenanthroxazole* (II*c*), m. p. about 231° (becoming reddish-brown on further heating), insoluble in dilute and in concentrated hydrochloric acid, soluble in boiling aqueous sodium hydroxide to a reddish-brown solution (Found: C, 76·4; H, 4·9. $C_{22}H_{17}O_3N$ requires C, 76·9; H, 5·0%).

p-*Chlorobenzaldehyde.* A solution of the imine (1 g.) and *p*-chlorobenzaldehyde (4 g.) in benzene (50 c.c.) was exposed to sunlight for 1 day (August). The crystals formed were recrystallised from benzene, giving colourless 2-*hydroxy*-2-p-*chlorophenyl*-2 : 3-*dihydrophenanthroxazole* (II*d*) in almost quantitative yield, m. p. about 221° to a red-brown melt, easily soluble in hot alcohol and hot benzene and soluble in concentrated sulphuric acid to an olive-green solution after some minutes (Found: C, 72·3; H, 3·9; N, 4·05; Cl, 10·5. $C_{21}H_{14}O_2NCl$ requires C, 72·5; H, 4·0; N, 4·0; Cl, 10·2%).

Piperonal. The imine (0·5 g.) and piperonal (1 g.) in benzene (50 c.c.) were exposed for 4 days (end of February); no crystals were formed. The benzene was driven off in a vacuum, and the residue washed with dilute sodium bicarbonate solution and crystallised from benzene. 2-*Hydroxy*-2-(3′ : 4′-*methylenedioxyphenyl*)-2 : 3-*dihydrophenanthroxazole* (II*e*) formed colourless crystals, m. p. 236° (decomp.) (Found: C, 73·4; H, 4·4; N, 4·25. $C_{22}H_{15}O_4N$ requires C, 74·0; H, 4·2; N, 3·9%).

2-*Methoxy*-1-*naphthaldehyde.* The imine (0·5 g.) and the aldehyde (1 g.), dissolved in benzene (30 c.c.), were exposed for a fortnight (September); no crystals were formed. The benzene was removed in a vacuum, and the residue washed with a small amount of benzene and crystallised from benzene. The almost colourless crystals (about 0·2 g.), m. p. 217°, of 2-*hydroxy*-2-(2′-*methoxy*-1′-*naphthyl*)-2 : 3-*dihydrophenanthroxazole* (II*f*) were difficultly soluble in cold alcohol. When it was treated with concentrated sulphuric acid at room temperature, an orange colour was obtained (Found: C, 79·2; H, 5·1; N, 3·3. $C_{24}H_{19}O_3N$ requires C, 79·4; H, 4·8; N, 3·6%).

Action of Heat on 2-*Hydroxy*-2-*phenyl*-2 : 3-*dihydrophenanthroxazole.*—The pyrolysis was carried out in a stream of dry carbon dioxide in a vessel fitted with a long side tube externally cooled; the vessel was immersed in a bath of ethyl cinnamate (b. p. 271°). An almost colourless deposit formed, together with drops of water (blue colour with anhydrous copper sulphate), on the walls of the side tube. The deposit, after crystallisation from benzene, showed no depression of m. p. when mixed with authentic 2-phenylphenanthroxazole prepared according to Stein and Day (*loc. cit.*) (Found: C, 85·2; H, 4·9; N, 4·8. Calc. for $C_{21}H_{13}ON$: C, 85·4; H, 4·4; N, 4·8%).

Action of Selenium and Air on 2-*Hydroxy*-2-*phenyl*-2 : 3-*dihydrophenanthroxazole.*—A mixture of the material (0·1 g.) and precipitated selenium (1 g.) (B.D.H.) was heated at about 300° (bath temp.) in a 50 c.c. distillation flask fitted with a capillary; the side tube was connected with an air condenser and air was sucked through the capillary. After 10 minutes' heating, suction was continued for 2 hours while the bath cooled. The colourless crystals deposited on the neck of the flask proved to be benzoic acid.

Action of Chromium Trioxide on 2-*Hydroxy*-2-p-*anisyl*-2 : 3-*dihydrophenanthroxazole.*—To the phenanthroxazole (3·2 g.), partly dissolved in glacial acetic acid (15 g.), a hot solution of chromium trioxide (8 g.) in glacial acetic acid (20 g.) was gradually added; the mixture boiled vigorously. It was poured into water (250 c.c.) after cooling, and the orange precipitate collected (pump) and extracted with hot concentrated sodium bisulphite solution. To the filtered solution, dilute sulphuric acid was added; the orange precipitate thus obtained, after crystallisation from alcohol, gave phenanthraquinone (0·8 g.).

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51. *Organic Sulphur Compounds. Part XXVIII. Thiono-thiol Tautomerism manifested by Sulphur Analogues of Cyclic Acid Anhydrides.*

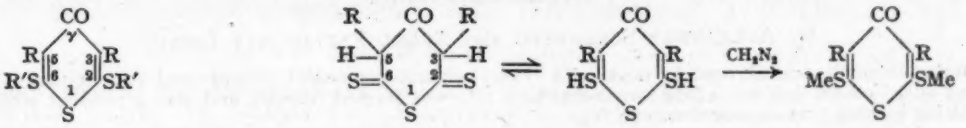
By ALEXANDER SCHÖNBERG and (MISS) WAFFIA ASKER.

The tautomeric changes (II ⇌ III) are discussed. Substances (II) are deep orange and form (*e.g.*, with diazomethane) colourless products of the general formula (I, R and R′ = univalent residue).

APITZSCH (*Ber.*, 1904, **37**, 1599; 1905, **38**, 2888; 1908, **41**, 4028) has stated that ketones of the general type $R{\cdot}CH_2{\cdot}CO{\cdot}CH_2R$ react with carbon disulphide in the presence of potassium hydroxide with the formation of orange-red substances of the general formula (III, R = univalent residue). He stated that compounds (III), when allowed to react with sodium methoxide, form the sodium salts, which, with methyl iodide, propyl chloride, benzyl chloride and so on, form colourless or almost colourless substances of the general formula (I, R = univalent residue).

According to modern views on the relationship between colour and constitution, it is very improbable that substances of constitution (III) are deeply coloured, whereas the derivatives, *e.g.*, the dimethyl ethers (IV), are colourless. Moreover, there is no reason why substances of constitution (III) should be deeply coloured.

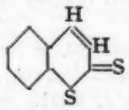
We believe that the orange substances mentioned above are derivatives of 2 : 6-dithio-1-thiopyranone (II, R = H) and that in their solutions a thiono-thiol equilibrium exists (II ⇌ III). The orange colour



(I.) (II.) (III.) (IV.)

attributed to substances of structure (II) is in accordance with the colour of substances of similar constitution (see Table), which all (except VI*a*) contain, as (II) does, the group $\rangle C(=S)-C(=S)-SR$ (R = univalent residue). The lack of colour in (I) and the orange colour of (II) may be compared with the lack of colour in (VI*a*) and the orange colour of (V*a*) (Schönberg and co-workers, *Ber.*, 1931, **64**, 2582),

TABLE.

Me—C(=S)—SH	Red-yellow	α-$C_{10}H_7$—C(=S)—S·S—C(=S)—$C_{10}H_7$(α)	Red	$CHPh_2$—C(=S)—SPh (V*a*.)	Orange
Ph—C(=S)—SH	Violet-red		Red	CPh_2=C(SH)·SPh (VI*a*.)	Colourless

Very little is known about thiono-thiol tautomerism. The text books concerned with tautomerism hardly mention this type, as there is a great tendency for the substances in question to react in the thiol form only. The problem arises, why substances of the general formula (II) are stable. It seems quite possible that the stabilisation is due to resonance and that these substances have to be regarded as resonance hybrids involving the forms (II), (V), and (VI).

The supposed equilibrium (II ⇌ III) explains why colourless or light yellow substances are obtained from the orange-red substances, not only in the cases mentioned by Apitzsch and co-workers (see above) but also by the action of diazomethane, diphenyldiazomethane, and piperidine. For instance, we found that the orange compounds (II, R = Ph or CO_2Et) yield the colourless compounds (IV, R = Ph or CO_2Et). We obtained, by the action of piperidine on (II, R = Ph), a yellow crystalline substance soluble in cold water and decomposing on heating with the splitting of piperidine; we advance for this substance the formula of a salt [compare (VII)].

(V.) (VI.) (VII.)

EXPERIMENTAL.

Action of Diazomethane on 2 : 6-*Dithio*-3 : 5-*diphenyl*-1-*thio*-γ-*pryanone* (II, R = Ph).—An ethereal solution of diazomethane (*Org. Syn.*, Vol. XV, 3) was added to the deep red ethereal solution of (II, R = Ph). Vigorous evolution of gas was observed and the mixture was kept at 0° for 24 hours. The product was crystallised from ligroin (b. p. 100—150°) and proved to be the colourless 2 : 6-bismethylthio-3 : 5-diphenyl-1-thio-γ-pyrone (IV, R = Ph), m. p. not depressed by an authentic specimen (Apitzsch, *Ber.*, 1904, **37**, 1607).

Action of Diphenyldiazomethane on 2 : 6-*Dithio*-3 : 5-*diphenyl*-1-*thio*-γ-*pyranone* (II, R = Ph).—To a warm benzene solution (30 c.c.) of (II, R = Ph) (1 g.), a benzene solution of diphenyldiazomethane [prepared from benzophenone-hydrazone (1·5 g.) (Staudinger and co-workers, *Ber.*, 1916, **49**, 1928)] was added. Vigorous evolution of gas took place and the mixture was kept for 1 day at room temperature, the solvent then being driven off and the residue crystallised from alcohol. Almost colourless crystals of 2 : 6-*bisbenzhydrylthio*-3 : 5-*diphenyl*-1-*thio*-γ-*pyrone* (I; R = Ph, R′ = $CHPh_2$), m. p. 162°, were obtained. The substance was freely soluble in benzene, and dissolved with difficulty in cold ether and cold ligroin (b. p. 100—110°) (Found: C, 77·8; H, 4·9. $C_{43}H_{32}OS_2$ requires C, 78·2; H, 4·8%).

Action of Piperidine on 2 : 6-*Dithio*-3 : 5-*diphenyl*-1-*thio*-γ-*pyranone* (II, R = Ph).—The pyranone derivative (1 g.) was dissolved in acetone (15 c.c.) and refluxed for 1 hour with piperidine (10 c.c.). After cooling, the crystals formed were collected and washed with acetone, in which (II, R = Ph) is freely soluble. The light yellow crystals of *dipiperidinium* 2 : 6-*disulphydryl*-3 : 5-*diphenyl*-1-*thio*-γ-*pyrone* (VII) dissolved with difficulty in ether, turned orange at about 180°, and melted at about 200° with the splitting of piperidine. They were soluble in cold water and on addition of dilute sulphuric acid an orange deposit was formed (Found: C, 65·0; H, 6·9; N, 5·2; S, 19·3. $C_{27}H_{34}ON_2S_3$ requires C, 65·0; H, 6·8; N, 5·6; S, 19·2%).

The thermal decomposition of the substance was accomplished in a closed apparatus which allowed the liberated piperidine to condense and the decomposition was carried out in a boiling nitrobenzene bath. The product was identified as piperidine by means of the picrate.

Action of Diazomethane on Ethyl 2 : 6-*Dithio*-1-*thio*-γ-*pyranone*-3 : 5-*dicarboxylate* (II, R = CO_2Et).—To the substance (2 g.), dissolved in ether, an ethereal solution of diazomethane was added, and the mixture kept at 0° for 24 hours. The product separated from alcohol in colourless crystals, m. p. 81—82°. It gave no depression with authentic ethyl 2 : 6-bismethylthio-1-thio-γ-pyrone-3 : 5-dicarboxylate (IV, R = CO_2Et) (Apitzsch, *Ber.*, 1908, **41**, 4033) (Found: C, 45·1; H, 4·8. Calc. for $C_{13}H_{16}O_5S_3$: C, 44·8; H, 4·6%).

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52. *Preparation of αζ-Diphenylhexatriene and 1 : 4-Diphenylbenzene from Cinnamaldehyde.*

By Alexander Schönberg and Abdel Fattah Aly Ismail.

Cinnamaldehyde was allowed to react with thionyl chloride or oxalyl chloride and the product (I) was treated with sodium iodide; αζ-diphenylhexatriene (II) was formed directly and also a product which on distillation yielded 1 : 4-diphenylbenzene (V).

The preparation of αζ-diphenylhexatriene (II) has previously been effected by various methods, none of which was satisfactory as regards yield, and in most cases a number of intermediate products were formed from the initial material, cinnamaldehyde. Smedley (J., 1908, **93**, 373) condensed cinnamaldehyde with sodium phenyl*iso*crotonate and obtained (II); from 35 g. of phenyl*iso*crotonic acid, 2 g. of the hydrocarbon were obtained.

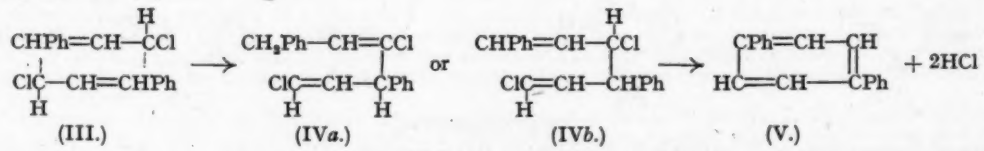
Farmer, Laroia, Switz, and Thorpe (J., 1927, 2955) used *s*-distyrylethylene glycol, which may be obtained in 10—12% yield from cinnamaldehyde. The next step, which further decreased the yield, as it proceeded by no means quantitatively, was the formation of dibromo-αζ-diphenylhexatriene, from which the hydrocarbon (II) was obtained in 60—65% yield by the action of zinc dust.

Kuhn and Winterstein (*Helv. Chim. Acta*, 1928, **11**, 87) prepared (II) by the action of potassium iodide in acetone on dibromo-αζ-diphenylhexatriene.

Styryldichloromethane (I), easily obtainable from cinnamaldehyde, is an obvious starting material for the preparation of (II). It was indeed used by Kuhn and Winterstein (*loc. cit.*), who treated it with zinc dust in alcohol, but obtained a very poor yield (quoted from *Centr.*, 1928, I, 1401; we could not consult the original paper). We found that, if the crude product (I) obtained by the action of thionyl chloride or oxalyl chloride on cinnamaldehyde is treated with sodium iodide in acetone, αζ-diphenylhexatriene (II) is formed, in addition to a product which on distillation yields 1 : 4-diphenylbenzene (V). By this method, it is now possible to obtain (II) and (V) in reasonable yields without isolation of intermediate products.

$$2CHPh{:}CH{\cdot}CHO \xrightarrow[SOCl_2]{(COCl)_2\ or} \underset{(I.)}{2CHPh{:}CH{\cdot}CHCl_2} \xrightarrow{NaI} \underset{(II.)}{CHPh{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CHPh}$$

Kuhn and Winterstein (*Ber.*, 1927, **60**, 432) have obtained 1 : 4-diphenylbenzene (V), and discussed two explanations for its formation. In our case, too, several explanations are possible; one may assume, for example, that by the action of sodium iodide on (I) the compound (III) is formed, which has the nature of a free radical; two of these radicals may add to each other to form (IV*a*) or (IV*b*), which on pyrolysis yields 1 : 4-diphenylbenzene (V):



(III.) (IV*a*.) (IV*b*.) (V.)

Experimental.

αζ-Diphenylhexatriene (II).—Freshly distilled cinnamaldehyde (30 g.) was refluxed with thionyl chloride (100 c.c.) or, preferably, oxalyl chloride (42 g.) (Staudinger, *Ber.*, 1909, **42**, 3975) for 10 hours (calcium chloride guard-tube). (Thionyl chloride is more accessible than oxalyl chloride, but the latter seems to yield purer products.) The excess of the reagent was then driven off in a vacuum, and the oily product dissolved in acetone (100 c.c.) and poured into a solution of sodium iodide (100 g.) in acetone (750 c.c.); the acetone used was free from alcohol and water. The mixture was refluxed (mechanical stirrer) for 4 hours, sodium chloride being precipitated, and then cooled, and the precipitate collected and washed several times with acetone. The filtrate and washings were evaporated to about 400 c.c. and cooled in ice. The precipitated green crystals were collected, and the acetone solution diluted with ice-water (about 400 c.c.); sulphur dioxide was passed through the mixture till the colour of the iodine was discharged; the dark semi-solid (A) was separated by decantation from the aqueous acetone solution (B) and treated with ether (about 100 c.c.). The solid (C) dispersed in the ethereal mixture was filtered off (2 g. of crude αζ-diphenylhexatriene); the ethereal filtrate was added to (B), and the whole shaken with ether (about 500 c.c.). The ethereal layer was washed successively with excess of sodium bicarbonate solution, water, 20% sodium thiosulphate solution (100 c.c.), and water, dried over sodium sulphate, and evaporated on the water-pump to about 100 c.c.; the yellow crystals (D) which separated on cooling were filtered off (1·1 g. of almost pure αζ-diphenylhexatriene). From the ethereal filtrate an additional quantity of less pure substance (E) was isolated by slow concentration, cooling and filtration, leaving a dark ethereal solution (F). C, D, and E crystallised from acetone in yellow plates (2·2 g.), m. p. 200°, not depressed by two authentic samples prepared according to Kuhn and Winterstein (*Helv. Chim. Acta*, 1928, **11**, 87), and Farmer, Laroia, Switz, and Thorpe (*loc. cit.*) (Found: C, 92·6; H, 7·0. Calc. for $C_{18}H_{16}$: C, 93·1; H, 6·9%).

1 : 4-*Diphenylbenzene* (V).—Solution (F) (in a 50 c.c. short-necked Claisen flask) was freed from ether, and the residue heated at about 150° (bath temp.) with occasional stirring for 1 hour, hydrogen chloride being evolved; the residue was distilled (direct flame) under about 45 mm. and the fraction distilling at about 250° (compare Schmidt and Schultz, *Annalen*, 1880, **203**, 124) was collected as a light brown oil which soon solidified. It separated from benzene (2 vols.)–alcohol (1 vol.) in colourless crystals (2·9 g.), m. p. 209—210°, not depressed by authentic 1 : 4-diphenylbenzene (Kuhn and Winterstein, *Ber.*, 1927, **60**, 432) (Found: C, 93·9; H, 6·0. Calc. for $C_{18}H_{14}$: C, 93·9; H, 6·1%).

Fouad I University, Abbassia, Cairo. [*Received, October 21st*, 1944.]

53. *Studies in the Anthracene Series. Part II.* The Action of Grignard Reagents on Dianthraquinone. New Derivatives of 9 : 9′-Dianthranyl.*

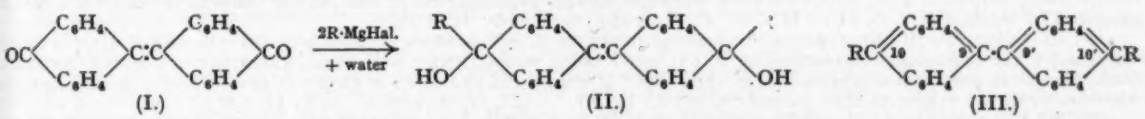
By Alexander Schönberg and Abdel Fattah Aly Ismail.

Dianthraquinone (I) reacts with Grignard reagents; the products on hydrolysis give *inter alia* compounds of type (II). (II; R = Ph, *o*-C_6H_4Cl, or α-$C_{10}H_7$), on pyrolysis or on reaction with glacial acetic acid in presence of acetic anhydride, loses two hydroxyl groups and gives (III; R = Ph, *o*-C_6H_4Cl, or α-$C_{10}H_7$), but with the same reagent (II; R = CH_2Ph) loses two molecules of water and gives (V).

Comparatively little is known about the chemistry of 9 : 9′-dianthranyl derivatives (III) and derivatives of dianthranene (II †) in spite of the possibility of their showing carcinogenic activity.

Barnett and Cook (J., 1923, **123**, 2631) prepared 10 : 10′-diphenyl-9 : 9′-dianthranyl (III; R = Ph) from 9-phenylanthrone, but the method is not of general application because homologues of the latter compound could not be obtained.

By the reaction of dianthraquinone (I), now easily available, with Grignard reagents, followed by hydrolysis, we have obtained 10 : 10′-*diphenyl*-, 10 : 10′-*di*-(o-*chlorophenyl*)-, 10 : 10′-*di*-(α-*naphthyl*)-, and 10 : 10′-*dibenzyl*-10 : 10′-*dihydroxydianthranene*. The first three compounds, on pyrolysis or on treatment with glacial acetic acid in presence of acetic anhydride, gave 10 : 10′-diphenyl-9 : 9′-dianthranyl, 10 : 10′-*di*-(o-*chlorophenyl*)- and 10 : 10′-*di*-(α-*naphthyl*)-9 : 9′-*dianthranyl* respectively.

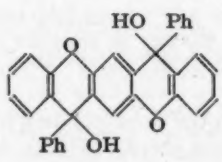


(I.) (II.) (III.)

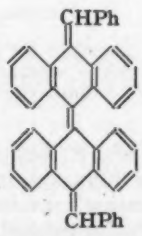
The elimination of two hydroxyl groups from a glycol by the action of glacial acetic acid has already been effected by Schönberg and Michaelis (J., 1935, 1403) in the case of (IV).

Substance (II; R = Ph, *o*-C_6H_4Cl, or α-$C_{10}H_7$) simulates (IV) in so far as (IV) also loses two hydroxyl groups on pyrolysis (Schönberg and Michaelis, *loc. cit.*).

10 : 10′-Dihydroxy-10 : 10′-dibenzyldianthranene (II; R = CH_2Ph) behaves somewhat differently from the other three compounds of type (II), since by the action of glacial acetic acid in presence of acetic anhydride two molecules of water are eliminated [compare the similar behaviour (elimination of water by hydrogen chloride) of benzyloxanthranol (Haller and Padova, *Compt. rend.*, 1905, **141**, 857)]; the compound produced, unlike the 9 : 9′-dianthranyl derivatives mentioned above, shows no fluorescence in benzene solution and is formulated as 10 : 10′-*dibenzylidenedianthranene* (V).



(IV.)



(V.)

Experimental.

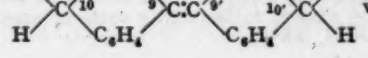
10 : 10′-*Dihydroxy*-10 : 10′-*diphenyldianthranene* (II, R = Ph).—To a solution of phenylmagnesium bromide (magnesium, 1·1 g.; bromobenzene, 7·2 g.; dry ether, 25 c.c.), dry benzene (50 c.c.) was added, and the mixture treated gradually with powdered dianthraquinone (I) (4 g.) (Schönberg and Ismail, *loc. cit.*). The solution immediately became olive-green, but after 4 hours' refluxing (with stirring), the ether being allowed to evaporate slowly, it had become orange-red and a yellow precipitate had formed. The cooled reaction mixture was poured into ammonium chloride–ice, the precipitate (A) collected, the benzene layer separated, washed, and dried, and the benzene evaporated. The residue was added to (A), and the whole material (3·6 g.) crystallised from ethyl acetate. It then separated from toluene in colourless prismatic crystals, m. p. above 300° (decomp.). It gave a blue-green coloration with concentrated sulphuric acid (Found: C, 88·9; H, 5·5. $C_{40}H_{28}O_2$ requires C, 88·9; H, 5·2%).

10 : 10′-*Diphenyl*-9 : 9′-*dianthranyl* (III, R = Ph) *from* (II, R = Ph).—(a) *By the action of glacial acetic acid in presence of acetic anhydride.* (II, R = Ph) (0·5 g.) was refluxed with glacial acetic acid (50 c.c.) and acetic anhydride (1 c.c.) for 2 hours (calcium chloride guard-tube). The end of the reaction was attained when a sample of the solid no longer gave the blue-green coloration with concentrated sulphuric acid given by the original material. The mixture was cooled, and the yellow solid collected (0·35 g.).

(b) *By pyrolysis.* (II, R = Ph) (1 g.) was heated in a vacuum in a boiling mercury bath for 2 hours. A small amount of the hydrocarbon sublimed and an additional quantity was obtained from the dark residue by extraction with boiling benzene, filtration, and evaporation (yield, 0·2 g.).

The products from (a) and (b) separated from benzene or toluene in pale yellow crystals identical with each other

* The publication of Schönberg and Ismail (J., 1944, 307) is regarded as Part I of this series.

† For the ring system:  we propose the name "dianthranene."

and with authentic 10 : 10′-diphenyl-9 : 9′-dianthranyl (Barnett and Cook, *loc. cit.*). The samples, separately or mixed, did not melt below 300°. The crystals prepared by the three methods had the same crystalline shape, the same green fluorescence in ultra-violet light (mercury vapour lamp), and the same blue-violet fluorescence in benzene or toluene solution; they gave no coloration with concentrated sulphuric acid, were very sparingly soluble in boiling ether and soluble in boiling toluene [Found for a sample prepared by method (a): C, 94·6; H, 5·5. Calc. for $C_{40}H_{24}$: C, 94·8; H, 5·2%].

The following compounds were prepared by methods substantially the same as those described above. 10 : 10′-*Dihydroxy*-10 : 10′-*di*-(*o-chlorophenyl*)*dianthranene* (reaction in hot solution): The precipitate corresponding to (A) was washed repeatedly with small quantities of acetone (4·5 g.) and then extracted twice with boiling xylene (250 c.c. each time). The xylene solution was filtered and cooled and the almost colourless, prismatic crystals formed were recrystallised from toluene; m. p. above 300° (decomp.). They gave a deep blue-green coloration with concentrated sulphuric acid (Found: C, 79·0; H, 4·6; Cl, 11·0. $C_{40}H_{26}O_2Cl_2$ requires C, 78·8; H, 4·3; Cl, 11·6%).

10 : 10′-*Di*-(*o-chlorophenyl*)-9 : 9′-*dianthranyl* separated from benzene in yellow crystals, m. p. above 300°, showing a deep green fluorescence in ultra-violet light and giving no coloration with concentrated sulphuric acid. Solutions in benzene or toluene showed a blue fluorescence [Found for a sample prepared by method (b): C, 82·9; H, 4·3; Cl, 12·3. $C_{40}H_{24}Cl_2$ requires C, 83·5; H, 4·2; Cl, 12·3%].

10 : 10′-*Dihydroxy*-10 : 10′-*di*-(*α-naphthyl*)*dianthranene* (reaction in hot solution): the final mixture of pale yellow deposit and deep red liquid was left overnight and then decomposed with ammonium chloride–ice. The precipitate formed was very sparingly soluble in acetone, benzene, toluene, or xylene, and crystallisation therefrom seemed to be accompanied by decomposition, since the solutions gave, on concentration, a deep blue-violet fluorescence characteristic of the corresponding hydrocarbon (III, R = α-$C_{10}H_7$). The product gave a green-blue coloration with concentrated sulphuric acid and its m. p. was above 300°. It was used without further purification for the preparation of 10 : 10′-*di*-(*α-naphthyl*)-9 : 9′-*dianthranyl*. This separated from toluene (to which it imparted a blue-violet fluorescence) in small yellow crystals, m. p. above 300°, which gave a bright green fluorescence in ultra-violet light, no coloration with concentrated sulphuric acid, and were very sparingly soluble in boiling ether and boiling benzene [Found for a sample prepared by method (a): C, 94·4; H, 5·5. $C_{48}H_{30}$ requires C, 95·0; H, 5·0%].

10 : 10′-*Dihydroxy*-10 : 10′-*dibenzyldianthranene* (reaction in hot solution; more benzene was added after ½ hour's refluxing): the precipitate corresponding to (A), after being washed twice with small quantities of acetone, separated from benzene in pale yellow crystals, m. p. about 300° (decomp. and evolution of gas). It gave a bright green coloration with concentrated sulphuric acid (Found: C, 88·6; H, 5·7. $C_{42}H_{32}O_2$ requires C, 88·7; H, 5·6%).

10 : 10′-*Dibenzylidene*-9 : 9′-*dianthranene* (V).—(II, R = CH_2Ph) (1 g.) was refluxed with glacial acetic acid (25 c.c.) and acetic anhydride (25 c.c.). The material dissolved on boiling, but after about 15 minutes reprecipitation occurred. Refluxing was continued for 2 hours, the mixture cooled, and the deep yellow product filtered off (0·45 g.). An additional quantity was obtained from the mother-liquor. Recrystallised from benzene, it formed yellow crystals which darkened (decomp.?) at about 230° and were sparingly soluble in ether (Found: C, 94·2; H, 5·5. $C_{42}H_{28}$ requires C, 94·7; H, 5·3%).

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54. *Preparation of* 1 : 5- *and* 1 : 8-*Naphthylenediamine and Related Compounds.*

By HERBERT H. HODGSON and JOHN S. WHITEHURST.

New methods are described for the preparation of 1 : 5- and 1 : 8-naphthylenediamine, both from 1 : 5- and 1 : 8-dinitronaphthalene separately and also from the mixture of diamines obtained by reduction of a mixture of 1 : 5- and 1 : 8-dinitronaphthalene. Improved methods of preparation of these dinitro-compounds are included.

THE preparation of 1 : 5- and 1 : 8-naphthylenediamine from the corresponding dinitronaphthalenes, described somewhat scantily in the literature, is readily effected by iron powder (Hodgson and Marsden, J., 1944, 398) in neutral aqueous suspension containing either ferrous or ferrous ammonium sulphate as catalyst. When a mixture of 1 : 5- and 1 : 8-dinitronaphthalene has been thus reduced, the diamines can be readily separated by preliminary conversion into a mixture of naphthalene-1 : 5- and -1 : 8-di-*p*-toluenesulphonamides, which is either (*a*) treated with aqueous potassium hydroxide to dissolve the 1 : 5-isomeride, or (*b*) extracted with toluene to dissolve the 1 : 8-compound.

EXPERIMENTAL.

1 : 5-*Naphthylenediamine*.—A mixture of pure 1 : 5-dinitronaphthalene (20 g.), iron powder (pin-dust, 60 g.), crystallised ferrous sulphate (6·0 g.), and water (200 c.c.) was refluxed for 3 hours, and then cooled in ice-water with continuous shaking. After filtration, the residue was extracted with boiling alcohol (200 c.c., charcoal), and the extract filtered hot; 1 : 5-naphthylenediamine (7 g.) separated from the filtrate in colourless needles, m. p. 190·5°, after recrystallisation from alcohol or pyridine (Bucherer and Uhlmann, *J. pr. Chem.*, 1909, **80**, 212, give m. p. 189·5°) (Found: N, 17·8. Calc.: N, 17·7%). The diamine was stable when pure and dry, but the presence of moisture promoted oxidation. The diacetyl and the dibenzoyl derivative had m. p. above 360° and 350°, respectively, agreeing with those recorded by Kunckell and Schneider (*Chem.-Ztg.*, 1912, **36**, 1021) and Sachs (*Ber.*, 1906, **39**, 3024).

1 : 5-*Diformamidonaphthalene*, formed by heating the diamine (0·8 g.) in 90% formic acid on the water-bath for 30 mins., was deposited, on cooling, in colourless rods, m. p. 280° after recrystallisation from 90% formic acid (Found: N, 13·0. $C_{12}H_{10}O_2N_2$ requires N, 13·1%).

1 : 5-*Dibenzylideneaminonaphthalene* separated immediately in fine needles when a solution of the diamine (1 g.) in alcohol (18 c.c.) and glacial acetic acid (6 c.c.) was treated dropwise with benzaldehyde; it crystallised from pyridine in pale yellow rhombs, m. p. 193° (Found: N, 8·45. $C_{24}H_{18}N_2$ requires N, 8·4%).

Naphthalene-1 : 5-*di*-*p*-*toluenesulphonamide* was formed when 1 : 5-dinitronaphthalene (20 g.) was reduced and extracted as above with alcohol (250 c.c., charcoal), and the hot extract stirred with finely powdered *p*-toluenesulphonyl chloride (20 g.), followed dropwise by pyridine (20 c.c.); it separated in almost colourless needles (22 g.), m. p. 318°, after recrystallisation either from pyridine, diluted subsequently with an equal volume of water, or from nitrobenzene (Found: N, 6·25. $C_{24}H_{22}O_4N_2S_2$ requires N, 6·0%).

Naphthalene-1 : 5-*di*-m-*nitrobenzenesulphonamide*, obtained similarly, crystallised in colourless needles (24 g.), m. p. 302°, from pyridine or nitrobenzene (Found : N, 10·5. $C_{22}H_{14}O_8N_4S_2$ requires N, 6·0%).

These two disulphonamides may also be purified by solution in the minimum quantity of 10% aqueous potassium hydroxide, followed by addition of solid potassium hydroxide until the separation of the crystalline dipotassium salts is complete. The crystalline mass is collected, dissolved in water, and decomposed.

Naphthalene-1 : 5-*di*-p-*toluenesulphondimethylamide* was obtained when the above sulphonamide in 2N-sodium hydroxide was stirred with methyl sulphate for 1 hour; the precipitate, after extraction with 2N-sodium hydroxide to remove any unmethylated compound, crystallised from nitrobenzene in small colourless plates, m. p. 275° (Found : N, 5·8. $C_{26}H_{26}O_4N_2S_2$ requires N, 5·7%).

Naphthalene-1 : 5-*di*-m-*nitrobenzenesulphondimethylamide*, prepared similarly, crystallised from nitrobenzene in small colourless plates, m. p. 315° (Found : N, 10·2. $C_{24}H_{18}O_8N_4S_2$ requires N, 10·1%).

1 : 8-*Naphthylenediamine*.—Pure 1 : 8-dinitronaphthalene (30 g.) was boiled for 3 hours with iron powder (90 g.), ferrous sulphate (9 g.), and water (200 c.c.), alcohol (120 c.c.) and charcoal added, and boiling continued for 30 minutes. The liquid was filtered and cooled in ice-water, and the colourless needles of 1 : 8-naphthylenediamine recrystallised from 30% alcohol; m. p. 66°, in agreement with De Aguias (*Ber.*, 1864, **7**, 309) and Meyer and Müller (*Ber.*, 1897, **30**, 775) (Found : N, 17·8. Calc. : N, 17·7%). The sulphate was precipitated in over 80% yield by extracting the dried residue from the dried reduction residue with boiling ether (1·1) and adding concentrated sulphuric acid in the required amount, or, alternatively, by adding alcohol to the reduction mixture so as to bring the solution to 30% strength, boiling it, filtering it hot, and precipitating the sulphate with dilute sulphuric acid.

Naphthalene-1 : 8-*di*-p-*toluenesulphonamide* was prepared by addition of *p*-toluenesulphonyl chloride (26·5 g., 10% excess) to a hot solution of the diamine (10 g.) in 30% alcohol (200 c.c.) with subsequent addition of anhydrous sodium carbonate until the mixture was just permanently alkaline; the reaction required *ca.* 30 minutes. The sodium derivative which separated (26 g.) was heated with 10% hydrochloric acid (30 c.c.) on the water-bath for an hour; the disulphonamide thus obtained crystallised from toluene in colourless rhombs and from glacial acetic acid in colourless needles, m. p. 207° (Found : N, 5·9. $C_{24}H_{22}O_4N_2S_2$ requires N, 6·07%).

Naphthalene-1 : 8-*di*-m-*nitrobenzenesulphonamide* crystallised from toluene or ethylene dichloride in clusters of rods, m. p. 200° (Found : N, 10·4. $C_{22}H_{14}O_8N_4S_2$ requires N, 10·6%).

Separation of 1 : 5- *and* 1 : 8-*Naphthylenediamine*.—*Method* (1). The mixture of 1 : 5- and 1 : 8-dinitronaphthalene (10 g.) obtained by nitration of naphthalene or 1-nitronaphthalene was reduced as described, the solid residue extracted with boiling pyridine (75 c.c.), the filtered extract treated with *p*-toluenesulphonyl chloride (10 g.), and the mixture heated on the water-bath for 3 hours, cooled, and poured into 15% hydrochloric acid. The precipitate of naphthalene-1 : 5- and -1 : 8-toluenesulphonamide was removed and stirred with water (200 c.c.) during the gradual addition of a solution of potassium hydroxide (10 g.) in water (30 c.c.). The mixture was heated to 75° during 30 minutes, and the two phases then separated by filtration or decantation. The oily phase (? potassium salt) was rendered solid (5·5 g.) by keeping it in contact with hydrochloric acid (15%) on a water-bath for 6 hours or with the cold acid overnight and finally heating on the water-bath for 1 hour; the resulting naphthalene-1 : 8-di-*p*-toluenesulphonamide, crystallised from toluene and then from glacial acetic acid, formed colourless needles, m. p. 207° (Found : N, 5·9%). The filtered or decanted aqueous alkaline phase was acidified with dilute acetic acid, the precipitated naphthalene-1 : 5-di-*p*-toluenesulphonamide (2·6 g.) extracted with 70% acetic acid (20 c.c.), and the solid sulphonamide washed with water and dried; it crystallised from pyridine, on cautious dilution with water, in colourless needles, m. p. 324° (Found : N, 6·3%).

Method (2). The dried mixture of 1 : 5- and 1 : 8-disulphonamides, prepared as above, was boiled with toluene (60 c.c.), and the liquid filtered hot; the filtrate contained almost all of the 1 : 8- and the residue almost all of the 1 : 5-isomeride. Both compounds were purified and crystallised as above.

Improved Preparation of 1 : 5- *and* 1 : 8-*Dinitronaphthalene*.—*Method* (1) *for* 5-*nitro*-1-*naphthylamine and* 1 : 8-*dinitronaphthalene*. 1-Nitronaphthalene (100 g.), dissolved in cold sulphuric acid (350 c.c., *d* 1·84), was nitrated by the dropwise addition of a mixed acid containing nitric acid (37 c.c., *d* 1·42) and sulphuric acid (144 c.c., *d* 1·84) initially at 0°. Three-fourths of the mixed acid were added slowly and the last quarter more rapidly so long as a temperature of 35° was not exceeded. The mixture, from which crystals commenced to separate immediately nitration was complete, was heated gradually until solution had occurred (at 90—100°) and then run in a thin stream into water (1 kg.) containing ice (2 kg.). After 1 hour's stirring, the fine paste (essential for subsequent operations) was removed, washed with water, then with 5% aqueous ammonia until the washings were slightly alkaline, and again with water; finally water was added to bring the volume to 850 c.c. This suspension was heated to boiling with vigorous agitation, and treated with two-thirds of a hot solution of crystallised sodium sulphide (60 g.) and sulphur (15 g.) in water (120 c.c.), the remaining third being added gradually after the initial violent ebullition had abated. The mixture was kept boiling for 30 minutes and cooled, and the residue removed, boiled with hydrochloric acid (100 c.c., *d* 1·16) and water (600 c.c.), washed, and dried. The filtrate was neutralised with ammonia at 0° and kept for 12 hours for the 5-nitro-1-naphthylamine (10 g.) to separate. The residue of 1 : 8-dinitronaphthalene (45 g.), m. p. above 165°, was boiled with benzene (800 c.c.) and charcoal; the cooled filtrate yielded pure 1 : 8-dinitronaphthalene (45 g.), m. p. 170·5°.

Method (2), *for* 1 : 5-*dinitronaphthalene*. The procedure of method (1) was varied at the point where crystals began to separate, in that the mixture was not heated to effect solution before the pouring into water. The coarser neutral paste thus obtained was boiled with water (450 c.c.) during the portionwise addition during 1 hour of finely powdered, crystalline sodium sulphite (85 g.). All the 1 : 8-isomeride passed into solution, the coarser 1 : 5-isomeride being secured from attack.

Alternatively, when the sulphuric acid solution of the dinitro-compounds in method (1) at 90—100° was allowed to cool gradually to 70—80°, almost complete crystallisation of 1 : 5-dinitronaphthalene occurred; this was collected on asbestos and washed with 70% sulphuric acid and with water (yield, 20—30 g.; m. p. 200—205°, raised to 216° by recrystallisation from pyridine). The hot filtrate, which contained almost all the 1 : 8-dinitronaphthalene, was heated again to 90—100°, and run into ice and water, the resulting paste collected, washed as before, mixed with water to bring the volume to 700° c.c. and treated as in method (1) for 30 minutes with a solution of crystallised sodium sulphide (30 g.) and sulphur (7·5 g.) in water (50 c.c.); the hot mixture was cooled and after filtration the residue was extracted with hydrochloric acid as in method (1) to remove 5-nitro-1-naphthylamine (2·4 g.); the residue of 1 : 8-dinitronaphthalene, when crystallised from benzene, had m. p. 166°.

Setting Points of Mixtures of 1 : 5- *and* 1 : 8-*Dinitronaphthalene.*

1 : 5-Compound, %	100	90	80	70	60	50	40	30	20	10	0
1 : 8-Compound, %	0	10	20	30	40	50	60	70	80	90	100
S. p.	216°	196°	180°	168·5°	159°	151°	145°	141°	140°	152°	170°

Quantitative Mononitration of 1-Nitronaphthalene to show the Distribution of 1 : 5- and 1 : 8-Dinitronaphthalene.—1-Nitronaphthalene (5 g., recrystallised from glacial acetic acid) was dissolved in sulphuric acid (25 c.c., *d* 1·84) at 0° and treated during vigorous stirring with a solution at 0° of dried potassium nitrate (2·919 g.) in sulphuric acid (15 c.c., *d* 1·84). The mixture was maintained at 0° throughout the reaction, and kept at 0° for 24 hours before being allowed to warm gradually to room temperature. After filtration (sintered glass), the solid was washed with sulphuric acid (7 c.c., *d* 1·84), and air sucked through it for 1 hour; it was then washed with water and air-dried. The setting point (average of six readings) was 143° and corresponded, as shown by a composition–setting point diagram, to a mixture containing 36% of 1 : 5- and 64% of 1 : 8-dinitronaphthalene. The filtrate, when diluted with water, gave a negligible amount of precipitate, indicating that the solid collected contained the whole of the dinitration product.

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TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, October 25th*, 1944.]

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55. *Studies in the Detoxication of Catalyst Poisons. Part I. General Survey of Some Detoxicants.*

By EDWARD B. MAXTED.

The applicability of various per-acids for the detoxication of platinum hydrogenation catalysts poisoned by cystein, by β-thionaphthol (naphthalene-β-thiol), and by thiophen has been examined in a preliminary manner. Many of these reagents, including persulphuric, perphosphoric, perchromic, permolybdic, and pertungstic acids, have been found to be sufficiently active detoxicants to warrant further study.

THE general principles involved in the detoxication of catalyst poisons have already been discussed (J., 1940, 252; 1941, 132). Briefly, it has been found that the usual toxic character, towards metallic catalysts, of molecules containing catalytically poisonous elements such as sulphur is in general lost if the structure of the molecule is such that the normally toxic atom is associated with a completely shared electron octet. Thus, organic sulphides or thiols are toxic towards, for instance, platinum in catalytic hydrogenation, whereas sulphones or sulphonic acids are non-toxic :

Toxic.	$(R)C:\ddot{S}:C(R')$	$(R)C:\ddot{S}:H$
	Sulphide	Thiol.
Non-toxic (shielded type).	$(R)C:\overset{\overset{O}{\cdot\cdot}}{\ddot{S}}:C(R')$	$(R)C:\overset{\overset{O}{\cdot\cdot}}{\ddot{S}}:OH$
	Sulphone.	Sulphonic acid.

The conversion, *in situ*, of catalyst poisons into non-poisonous derivatives of shielded type constitutes a method of eliminating toxicity from impure systems without the necessity for actual removal of the poison by absorption or other means; and the method possesses considerable practical interest, since the removal, in the ordinary sense, of small traces of catalyst poisons from impure substances before, for instance, their hydrogenation is often difficult, particularly if the poisons are in a not easily absorbable form.

The present paper, which relates throughout to catalytic hydrogenation, contains a preliminary survey of some detoxicants for the treatment of three of the principal types of catalyst poisons containing sulphur, with the object of ascertaining what detoxicating reagents are suitable for more detailed study. Special attention has been given to the detoxication of cystein, since this has a structure similar to that of the albuminoid sulphur poisons present as impurities in the unsaturated glyceride oils, which are extensively hydrogenated in industry; but a shorter examination has also been made of the detoxication of a thiophenol and of thiophen, which are representative respectively of the sulphur poisons in industrial phenols and in technical benzene or naphthalene.

Since detoxication has, in practice, to be applied to a very small concentration of poison, contained as an impurity in an unsaturated substance, the detoxicating reagent should, as far as is possible, neither add on to the ethylenic or other unsaturated bonds of this unsaturated substance nor attack these bonds in such a way as to cause fission. In an earlier paper (*loc. cit.*) hypochlorites have been used as detoxicants. Hypochlorites and hypobromites are effective detoxicating agents for many sulphur poisons. There is, however, with these reagents, a considerable risk of halogenation of the unsaturated substance. The extent of this under favourable conditions has not yet been determined; but an apparently more valuable class of detoxicants, which can more readily be used in the presence of substances containing unsaturated bonds, has been found in various per-acids. With these, it is possible to apply detoxication either before or during hydrogenation.

In the present paper, the conversion of the poison into a shielded form has in every case been obtained by oxidation. Thus, the observed detoxication of cystein in all probability involves its passage into cysteinic acid, the sulphur atom of which has the saturated electronic configuration

$$HO:\overset{\overset{O}{\cdot\cdot}}{\ddot{S}}:CH_2\cdot CH(NH_2)\cdot CO_2H$$
$$\underset{\cdot\cdot}{O}$$

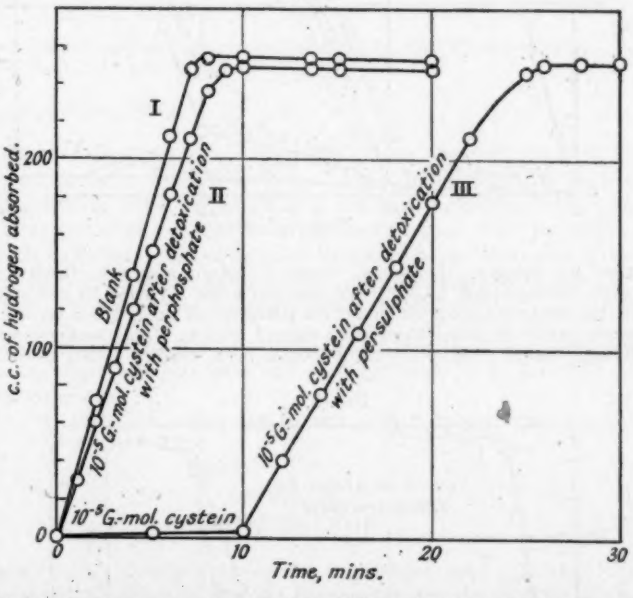
The unsaturated substance, to which the poison was added as an impurity, has consisted of crotonic acid. Platinum has, for convenience, been used throughout as the hydrogenation catalyst. The change of the poison into a non-toxic form would also apply to the hydrogenation of other unsaturated substances and to catalysis with other metals, *e.g.*, with nickel, save that, with oxidisable metallic catalysts, modifications in the actual detoxication procedure are of course necessary in order to maintain the hydrogenation catalyst in a reduced state. These will be dealt with in a later paper.

Experimental.

The standard hydrogenation charge introduced into the hydrogenation pipette consisted of 0·075 g. of stock platinum-black, 5 c.c. of a 2N-solution of crotonic acid in acetic acid, a further 3 c.c. of acetic acid and 2 c.c. of water, also the poison and the detoxicant, the water being used for extending the range of possible investigations to poisons or detoxicating reagents which are more conveniently applied in aqueous solution. The hydrogenation tests were carried out in a shaker, at 27° and under standardised conditions, the rate of absorption of hydrogen being followed in a gas burette in the usual way.

Detoxication of Cystein.—(i) *Use of persulphates.* The effect of adding a small quantity of a persulphate to the standard hydrogenation system previously poisoned with 10^{-5} g.-mol. of cystein is shown in Curve III of Fig. 1. The poisoned system was first shaken with hydrogen under standard conditions to determine the hydrogenation rate in the presence of the poison. The run was, after 10 minutes, interrupted and a small quantity of potassium persulphate (estimated at about 0·05 g.) was dropped into the hydrogenation pipette, which was removed from the thermostat and heated to 100° in a water-bath. The pipette was then re-cooled, re-attached to the hydrogenation apparatus, and, after the usual displacement of air by hydrogen, the run was continued at 27° under the same conditions as before. The detoxication effect caused by the persulphate is well seen by the abrupt change in the slope of the graph. It will also be seen that the total amount of hydrogen absorbed is approximately equal to the normal saturation value (250—260 c.c. at the prevailing temperature and pressure) of the amount of crotonic acid present, indicating little, if any, fission of the double bond of the unsaturated substance by the persulphate in addition to its detoxication of the cystein. Any excess of persulphate remaining as such after the detoxication could, even if it also undergoes hydrogenation to sulphate, only absorb a negligibly small volume of hydrogen, since the total hydrogen value of the whole of the persulphate added is only about 4 c.c.

Fig. 1.



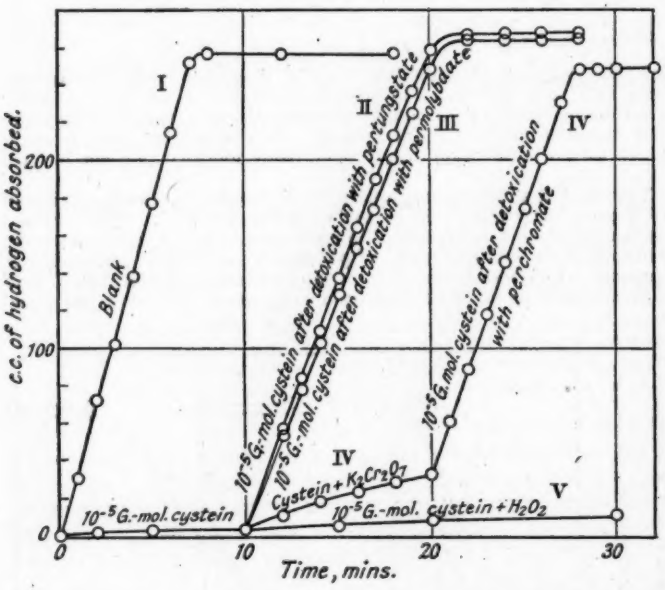
(ii) *Use of perphosphates.* The detoxicating reagent was in this case added directly as the acid. Permonophosphoric acid, H_3PO_5, is stated (Schmidlin and Massini, *Ber.*, 1910, **43**, 1162) to be formed by the interaction of phosphoric oxide with hydrogen peroxide. Accordingly, in this test, approximately 0·05 g. of phosphoric oxide was allowed to react at 0° with a few drops of hydrogen peroxide and the product was quickly mixed with a standard hydrogenation charge containing 10^{-5} g.-mol. of cystein. The mixture was heated, as before, to 100° to facilitate the oxidation of the poison and to destroy any excess of hydrogen peroxide, which quickly decomposed in the presence of the platinum catalyst with evolution of oxygen. The hydrogenation pipette containing the charge was then cooled to 27° and shaken with hydrogen. The high degree of detoxication brought about by this detoxicant is shown in Curve II of Fig. 1, the slope of which should be compared with that of the first part of Curve III (cystein without detoxication) and with Curve I, which is a blank run, without poison or detoxicant. From the figure, it would seem that perphosphoric acid is a more active detoxicating agent than a persulphate, although the conditions in these exploratory experiments—particularly from the standpoint of the amount of phosphoric oxide and hydrogen peroxide added—may not be strictly comparable with the persulphate run. It should be noted that both persulphates and perphosphates would be particularly suitable as detoxicating reagents, since they would leave as a residue only an innocuous sulphate or phosphate.

(iii) *Use of anions containing metals.* A further class of active detoxicating reagents consists of the unstable per-acids, or their salts, formed by the action of hydrogen peroxide on oxygenated anions containing metals. Most, if not all, of these metallic per-acids, especially perchromic, permolybdic, and pertungstic acids, have been shown to act as effective detoxicants. Peruranic, pervanadic, and other metallic per-acids were found to be less active; but it is not yet known whether this may have been due to toxic impurities (*e.g.*, traces of toxic foreign metals) in the specimens available. Even the per-acid formed from hydrogen peroxide and a permanganate is to some extent active, although the extent of the detoxication obtained is, at any rate in this case, almost certainly restricted by the known poisonous nature (J., 1940, 469) of the manganous salt to which the per-acid is probably reduced during the subsequent hydrogenation. Permanganates, in the absence of hydrogen peroxide, are only of about the same activity as dichromates (see later). Hydrogen peroxide, by itself, is almost inactive as a detoxicant; and this is also the case for perborates, which are not true per-acids.

Examples of detoxication by metallic per-acids are given in Fig. 2. Curve I is a blank run with the standard hydrogenation system containing no poison or detoxicant. In Curve II, 10^{-5} g.-mol. of cystein was added as the poison and hydrogenation was carried out for 10 minutes without detoxicant. At this point, the run was interrupted, and about 0·05 g. of ammonium tungstate and a few drops of hydrogen peroxide added under the same conditions as have already been given for detoxication by perphosphoric acid. The interrupted hydrogenation was then continued under standard conditions. The rise in the hydrogenation rate after the detoxication is shown by the graph after the first 10 minutes. Curve III, the first part of which (up to 10 mins.) is identical with the first part of Curve II, is a similar run with addition

of a permolybdate as the detoxicant. In Curve IV, about 0·05 g. of potassium dichromate, in the absence of hydrogen peroxide, was added after the first 10 minutes of the run, which, as in all cases in the figure, except the blank run, was with a system containing 10^{-5} g.-mol. of cystein. The extent of the detoxication with dichromate alone was not great (see the middle part, from 10 to 20 mins., of Curve IV); and, after a further 10 minutes, the usual few drops of hydrogen peroxide and a little additional potassium dichromate were added, since the chromium already present in the solution had been reduced to the green state, whereupon a sharp rise in the hydrogenation velocity occurred. The total volume of hydrogen absorbed was somewhat lower than usual, this being in agreement with the expected fission of the double bond of the crotonic acid by the dichromate, although the amount of this loss of unsaturated substance could not have been great on account of the small quantity of the chromium compound present. Curve V shows the effect of adding hydrogen peroxide alone. Little or no improvement in the hydrogenation rate occurred. The curve for the addition of sodium perborate was almost identical with Curve V and has therefore been omitted from the figure.

FIG. 2.



In place of adding these metallic per-acids during the progress of the run, they can of course be added before any hydrogenation is begun, as in Curve II of Fig. 1; and further experiments have shown that they are also effective if the metallic hydrogenation catalyst is absent during the detoxication treatment, although this catalyst assists the rapid destruction of any excess of hydrogen peroxide or of per-acid, which have otherwise to be removed by boiling. This detoxication in the absence of a hydrogenation catalyst is of importance if it is desired to use an oxidisable catalyst such as nickel for the subsequent hydrogenation.

Detoxication of β-Thionaphthol and of Thiophen.—Both of these poisons are susceptible to detoxication by the same reagents as have been used for cystein. However, whereas cystein responds directly, it was found necessary with thiophen, and helpful with thionaphthol, to apply the reagent after a period of preliminary hydrogenation, during which the poison present in the system is, by virtue of its preferential adsorption on the catalyst, preferentially hydrogenated to a derivative more easily oxidised than the original poison. This was expected from the known chemistry of thiophen, since its hydrogenated product, tetrahydrothiophen, readily forms a derivative of shielded type (a sulphone) on oxidation,

FIG. 3.

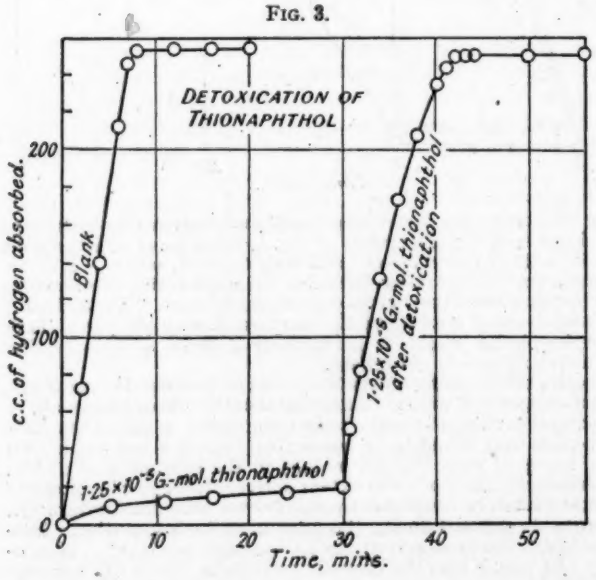
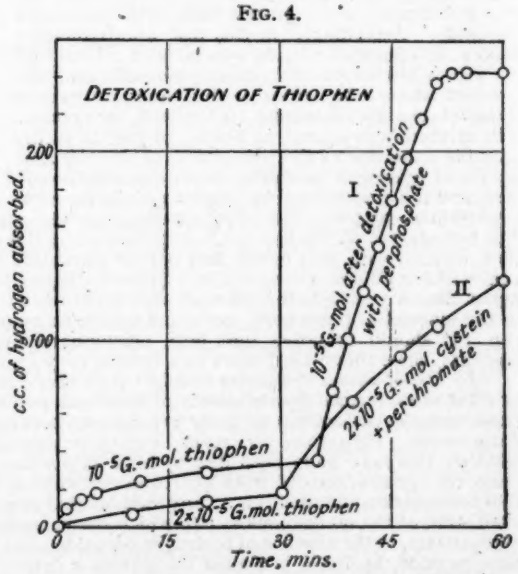


FIG. 4.



while thiophen itself is not easily attacked; but it was less expected for thionaphthol. It is not known whether the preliminary hydrogenation reduced one or both rings of the thionaphthol; but the non-toxic derivative formed by the detoxication process almost certainly consists of the corresponding sulphonic acid.

The detoxication, with perphosphoric acid, of $1{\cdot}25 \times 10^{-5}$ g.-mol. of β-thionaphthol contained in the standard hydrogenation system, the catalyst being 0·075 g. of platinum, as before, is shown in Fig. 3. After hydrogenation for 30 mins., at 27°, the detoxicating reagent was added under similar conditions to those already described and the run was then continued. As with cystein, the hydrogenation velocity rose steeply after the detoxication; but, both with thio-

naphthol and with thiophen (see Fig. 4), there was visible progressive coagulation of the platinum catalyst, which led to a slightly curved reaction path. This coagulation could of course have been avoided by using a supported catalyst. In accordance with previous experience, a perchromate gave a lesser degree of detoxication than a perphosphate, and a persulphate was less active still; but, since the amounts added were only approximately comparable, their exact relative detoxicating efficiencies are still to be determined.

Fig. 4 shows the detoxication of thiophen. In the run corresponding with Curve I, 10^{-5} g.-mol. of thiophen, contained in the standard hydrogenation system, was detoxicated, after 35 minutes, with perphosphoric acid. In Curve II, 2×10^{-5} g.-mol. of thiophen was detoxicated, after 30 mins., with perchromic acid.

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56. *Evidence for the Structural Isomerism of Hantzsch's Aryl* syn- *and* anti-*Diazotates.*

By HERBERT H. HODGSON and EWART MARSDEN.

In view of the fact that Hantzsch's aryl *syn*- and *anti*-diazosulphonates and aryl *syn*- and *anti*-diazocyanides are probably structural and not stereo-isomers, the evidence for the stereo- or structural isomerism of the aryl *syn*- and *anti*-diazotates is now examined. It is concluded from experimental evidence: (*a*) that the solid *syn*(normal)-diazotates are represented by the formula Ar·N:N·OM (where M is a metal), and in aqueous solution hydrolyse to give an equilibrium mixture, $Ar{\cdot}N{:}N{\cdot}OH \rightleftharpoons Ar{\cdot}\overset{+}{N}{\equiv}N{:}\}\bar{O}H$, the diazohydroxide being the coupling compound; (*b*) that the *anti*(or *iso*)-diazotates are either nitrosoamines, $Ar{\cdot}\bar{N}(NO)\}\overset{+}{M}$, or equilibrium mixtures in alkaline solution of the ionised normal diazotate and nitrosoamine,

$$Ar{\cdot}N{=}N{\cdot}\bar{O}\}\overset{+}{M} \rightleftharpoons Ar{\cdot}\bar{N}(NO)\}\overset{+}{M}.$$

IT is well known that when a mineral acid solution of a diazonium salt is treated gradually with sodium or potassium hydroxide in the cold, a marked change occurs in the properties of the diazo-compound as the acidity of the solution diminishes, and that change persists until the solution is markedly alkaline, although heat is sometimes necessary to consummate the final conversion. Three broad zones can clearly be distinguished, *viz.*, acid up to *ca.* pH 3·5, where diazonium salts can exist, neutral from *ca.* pH 6·5—8·0, where the so-called normal or *syn*-diazotates (hereinafter styled *n*-diazotates) are formed, and alkaline above pH 8·0, where *iso*- or *anti*-diazotates make their appearance. Whereas the constitution of the diazonium salts has long been settled in favour of Blömstrand's formula, $Ar{\cdot}\overset{+}{N}{\equiv}N{:}\}\bar{X}$, the structures of the *syn*- and *anti*-diazotates still await determination, despite discussion extending from 1866 to 1931 and recently revived by Farrar and Gulland (J., 1944, 368). The alternative points of view are:

(a) *Stereoisomeric*, due to Hantzsch (*Ber.*, 1894, **27**, 1702), whereby the isomers differ only in geometrical arrangement:

Normal or *syn*-diazotates — *iso*- or *anti*-Diazotates

(b) *Structural*, wherein many different versions occur, of which the most important are: (1) that the *n*-diazotates are obtained from a diazohydroxide Ar·N:N·OH, and the *iso*-diazotates are derived from the isomeric (tautomeric) nitrosoamine, Ar·N(NO)—H (cf. Schraube and Schmidt, *Ber.*, 1894, **27**, 514; v. Pechmann and Frobenius, *ibid.*, p. 672; Bamberger, *ibid.*, p. 679); (2) the structure, $Ar{\cdot}N{=}\underset{\downarrow}{N}{-}$ O, originally proposed rather speculatively by Bamberger and later supported with fresh evidence by Angeli (*Gazzetta*, 1921, **51**, i, 35; *Ber.*, 1926, **59**, 1400), for the *n*-diazotate ion, with the structure $Ar{\cdot}N{=}N{-}\bar{O}$ for the *iso*diazotate ion.

With respect to Hantzsch's stereochemical theory of the diazotates, Taylor and Baker (Sidgwick's "Organic Chemistry of Nitrogen," 1937, p. 417) state that the strongest evidence in its support is derived from the study of the two forms of the diazocyanides and the diazosulphonates, which until recently have been regarded as stereoisomers. It seemed logical, state Taylor and Baker (*ibid.*, p. 419), to assign the isomerism to a cause which was common to all three classes, and the only possible one was geometrical isomerism; they concluded, however, that without direct experimental evidence, Hantzsch's view remained a probable assumption and could not be taken as firmly established. Recently, however, Hodgson and Marsden (J., 1943, 470) have submitted experimental evidence indicating that Hantzsch's so-called *syn*- and *anti*-diazosulphonates were not geometrical but structural isomers, *viz.*, diazosulphites and diazosulphonates respectively, and later (J., 1944, 395) that the so-called *syn*- and *anti*-diazocyanides have the *iso*nitrile and the nitrile structure respectively. Thus geometrical isomerism in two of the three classes concerned is now invalid, and the analogy on which the stereochemical structures for the diazotates was based not only disappears, but must be used for a structural representation of the *n*- and *iso*-diazotates. Such a point of view will now be explored.

Normal or syn-*Diazotates.*—From the fact that only the *n*-diazotates couple with phenols and amines their structure can be settled from a study of the equilibria :

$$\underset{(a)}{Ar\cdot\overset{+}{N}\equiv N:\}\bar{O}H} \rightleftharpoons \underset{(b)}{Ar\cdot N=N\cdot OH} \xrightarrow{+NaOH} \underset{(c)}{Ar\cdot\overset{+}{N}=N-\bar{O}\}\overset{+}{Na}} + H_2O$$

which can be assumed to exist in the solution prior to coupling with an alkaline phenol. The anion (*c*) of the sodium salt can be rejected forthwith as the coupling reagent, since it is negatively charged and would be repelled from the *o*- and *p*-positions of the phenol; in fact, coupling can be retarded and almost prevented by increase of alkaline concentration. Choice of coupling reagent lies therefore between (*a*) and (*b*), and Conant and Tischler (" The Chemistry of Organic Compounds," The Macmillan Co., New York, 1939, p. 382) state that it is (*b*) which couples (cf. also Conant and Peterson, *J. Amer. Chem. Soc.*, 1930, **52**, 1220; Hodgson, *J. Soc. Dyers and Col.*, 1942, **58**, 228; Hodgson and Marsden, *ibid.*, 1944, **60**, 16, 120).

In further support of the above theory of coupling it has been found that *p*-nitrobenzeneazo-*N*-bromocarbonamide rapidly couples with either α- or β-naphthylamine in chloroform or benzene, *i.e.*, under conditions where a diazonium ion could not exist (cf. Hodgson and Marsden, J., 1944, 395). In solution, therefore, the so-called *n*-diazotates are equilibrium hydrolysis mixtures of ionised and un-ionised compounds :

$$Ar\cdot N=N-\bar{O}\}\overset{+}{Na} + H_2O \rightleftharpoons Ar\cdot N=N\cdot OH + NaOH$$

and in the solid state they have the configurations of an ordinary alkali salt capable of ready hydrolysis by water. This follows experimentally from the fact that the *n*-diazotates couple at once with α- or β-naphthol and with α- or β-naphthylamine when the latter compounds in finely divided form are stirred into an aqueous solution of the diazotate prepared by Bamberger's directions (*Ber.*, 1896, **29**, 461). Further, when the solid sodium salt of β-naphthol is added to the aqueous solution of the *n*-diazotate or when their solutions are mixed in either order, coupling occurs forthwith.

The previous data indicate that the formula of a *n*-diazotate is Ar·N=N·ONa, and confusion as to which is the real coupling reagent has led to this formula being assigned to the *iso*diazotate. It is only when the pH value of the solution is sufficiently high, *i.e.*, when hydrolysis to Ar·N=N·OH is prevented, that coupling is inhibited. This formula for the diazotate is also supported by the theories of Wistar and Bartlett (*J. Amer. Chem. Soc.*, 1941, **63**, 413) and Hauser and Breslow (*ibid.*, p. 418), which claim that the coupling reagent is the diazonium ion, from which it must follow that the relevant anion is either the hydroxyl group (in alkaline or neutral solution) or the anion of the weak acid employed in their buffer solutions. In no case could an anion of the Angeli type, $R-\underset{\downarrow}{N}=\bar{N}$ (O), be visualised.

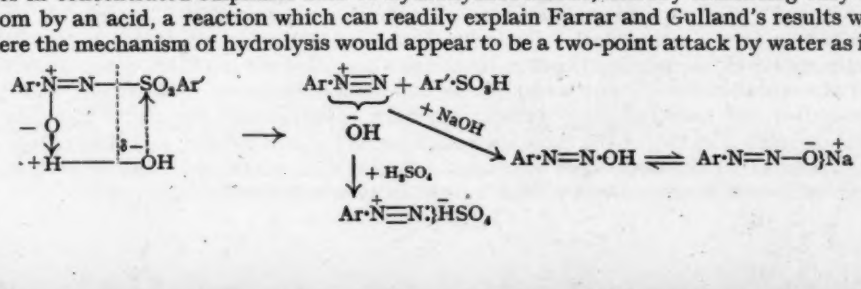
The counter arguments to Angeli's theory are collected together by Saunders (" The Aromatic Diazo-compounds," 1936, p. 209) and are very imposing : they include the oxidation of *n*-diazotates to salts of phenylnitroamine, which would be impossible on Angeli's constitution.

Farrar and Gulland (*loc. cit.*), however, have prepared azoxysulphones,

$$Ar\cdot\overset{O}{\overset{\|}{N}}\rightarrow N\cdot SO_2Ar' \longleftrightarrow Ar\cdot\overset{O}{\overset{\nearrow}{N}}=N\cdot SO_2Ar',$$

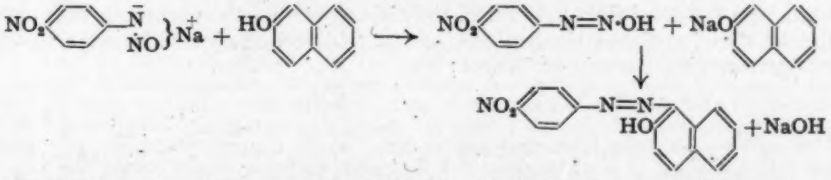
which, like Angeli's azoxycarbonamides (cf. Angeli, *Gazzetta*, 1917, **47**, I, 215; Pieroni, *ibid.*, 1922, **52**, II, 32), are readily hydrolysed by dilute alkali to *n*-diazotates. In addition, distillation of the azoxysulphones with 50% sulphuric acid affords considerable quantities of phenol, which indicates that a diazonium salt is an intermediate in the hydrolysis; further, when phenyl-*p*-tolylazoxysulphone is dissolved in ice-cold concentrated sulphuric acid, the solution on dilution with water exhibits the reactions of benzenediazonium sulphate. Farrar and Gulland state that, if it is accepted that the products of hydrolysis of all these azoxy-compounds are true *n*-diazotates, either these must be denoted by the Angeli formula above, or a transfer of oxygen from one nitrogen to the other must be postulated to give the formula Ar·N=N·ONa. They also state that there is neither analogy nor experimental support for this migration, but in any recognition of the Angeli theory recourse must be made to such a transfer, as in the explanation of the facile oxidation of *n*-diazotates to arylnitroamines.

It has long been known (Wallach and Belli, *Ber.*, 1880, **13**, 525; *Annalen*, 1882, **215**, 218) that azoxybenzene itself isomerises in concentrated sulphuric acid to hydroxyazobenzene, thereby indicating easy detachment of the oxygen atom by an acid, a reaction which can readily explain Farrar and Gulland's results with the azoxy-sulphones, where the mechanism of hydrolysis would appear to be a two-point attack by water as in the scheme :



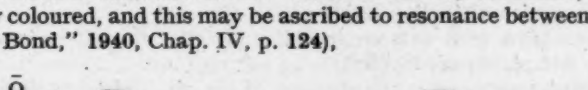
the resulting ephemeral diazonium hydroxide becoming diazonium sulphate in the acid hydrolysis and *n*-diazotate in the alkaline hydrolysis. In this respect the azoxysulphones behave like azoxycarbonamides in having the very stable N—S and N—C bonds in the parent diazosulphonate and diazo-carbonamide weakened by the dipolar $\overset{+}{N}—\overset{-}{O}$ group, which sets up adjacent positive charges at the N—S and N—C bonds respectively, with consequent destabilisation and rupture by hydrolysis (compare Pauling on the adjacent charge rule, "Nature of the Chemical Bond," Cornell Univ. Press, 1940, pp. 199, 210). The diazosulphonates and diazosulphides, like the diazocarbonamides and diazocyanides, will not couple with alkaline β-naphthol.

The acceptance of Angeli's formula for the *n*-diazotate, however, would involve facile migration of the oxygen from one nitrogen to the other and back according to circumstances, *i.e.*, tautomeric oxygen. Now the formula Ar·N=N·OH must be postulated for the hydroxide before conversion into the *n*-diazotate, whether it couples as such (Conant and Peterson, *loc. cit.*) or as the diazonium hydroxide (Wistar and Bartlett, *loc. cit.*). Further, if the sodium and silver salts of *p*-nitrodiazobenzene are treated with methyl iodide, the former give *p*-nitro-*N*-nitrosomonomethylaniline, and the latter the methyl ether of *p*-nitrobenzenediazohydroxide, $NO_2·C_6H_4·N=N·O·CH_3$, which shows the reactions of a diazo-compound by giving a diazoamino-compound with aniline and by coupling with phenol. In both cases the oxygen is attached to the outer and not to the inner nitrogen, and indicates a coupling mechanism involving scission at the N—O bond. Additional evidence of like import is given by the *N*-nitrosoacylarylamines, which behave like *n*-diazotates (cf. Grieve and Hey, J., 1935, 689; Hodgson and Marsden, J., 1943, 285) and couple following alkaline hydrolysis to the normal diazotate (Bamberger and Muller, *Annalen*, 1900, **313**, 126). A still more striking example is afforded by the mono-coupling of tetrazotised *p*-phenylenediamine with β-naphthol in concentrated sulphuric acid solution, which must take place at the N—O link of the structure, $:N\equiv\overset{+}{N}—C_6H_4—N=N—O—SO_3H$ ($\overset{}{}^{-}HSO_4$) (Schoutissen, *J. Amer. Chem. Soc.*, 1933, **55**, 4541), and should finally dispose of any doubt as to whether coupling occurs at the second nitrogen to which an oxygen atom had previously been attached. Conversion of these compounds into alkali *n*-diazotates would involve the reverse migration of oxygen from the outer to the inner nitrogen if Angeli's formula be postulated for the *n*-diazotate, and such facile migration in either direction appears to introduce an unnecessary complication for an otherwise simple reaction. Similarly, the more involved mechanisms put forward by Angeli to explain coupling and diazo-ether formation fall into the same category. The coupling of the sodium salt of the *p*-nitrophenylnitrosoamine caused by β-naphthol alone to form *p*-nitrobenzeneazo-β-naphthol could only take place *via* the sequence of changes :



thereby proving that the oxygen of the coupling reagent is attached to the outer nitrogen.

iso*Diazotates*.—This term has been used to refer to (*a*) those solutions of diazo-compounds which, owing to their high pH value, couple either very slowly or not at all with phenols and naphthols, and (*b*) nitrosoamines which in the cases of some amines, *e.g.*, *p*-nitroaniline, are made immediately by the action of alkali hydroxides on the diazonium salts, and in other cases, *e.g.*, aniline, require very concentrated (sometimes 60%) potassium hydroxide solution at about 140°. Solutions (*a*), with no or little coupling ability, are probably equilibrium mixtures of the sodium nitrosoamine and *n*-diazotate, $R·N=N—\overset{-}{O}\}\overset{+}{Na} \rightleftharpoons \underset{Na^+}{R·\overset{-}{N}}—NO$, in which the nitrosoamine greatly predominates. Compounds (*b*) are either the alkali nitrosoamines, which in alkaline solutions retain their structure, or are ion-pairs (cf. Hammett, "Physical Organic Chemistry," 1940, p. 40 *et seq.*), whose normal condition is that of the *n*-diazotate but which under the influence of heat and caustic alkali have been converted into the nitrosoamines. Both types react with methyl iodide to give *N*-nitrosomethylarylamine, but 1-chloro-2 : 4-dinitrobenzene in boiling benzene failed to react with the nitrosoamine from *p*-nitroaniline, thereby indicating the intensity of the electrostatic attraction. Incidentally, Wojciechowski (*Rocz. Chem.*, 1934, **14**, 739) reports that he was unable to get potassium *p*-chlorobenzene*iso*diazotate (nitrosoamine) free from caustic alkali, and our experience appears to indicate that the presence of a slight amount of caustic alkali is essential for the preservation of the *iso*diazotate. Some of the nitrosoamines, *e.g.*, from *p*-nitroaniline and *p*-chloroaniline, are highly coloured, and this may be ascribed to resonance between ionic structures (cf. Pauling, "Nature of the Chemical Bond," 1940, Chap. IV, p. 124),



Potassium benzene*iso*diazotate prepared according to the directions of Schraube and Schmidt (*loc. cit.*) was

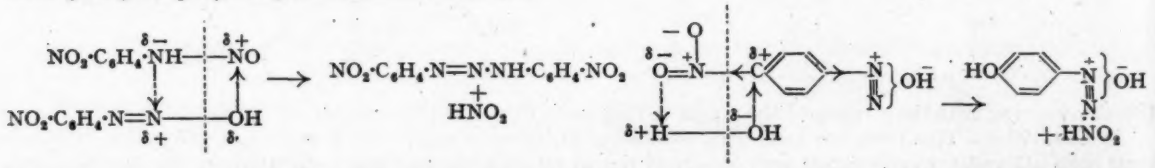
colourless initially but became brown rapidly and progressively; this is due possibly to incipient hydrolysis by atmospheric moisture with resultant generation of *n*-diazotate, which in turn would be in equilibrium with diazonium hydroxide, whose decomposition to phenol with subsequent coupling by the *n*-diazotate would produce the coloured azo-compound shown by the colour change above. Solid sodium and potassium *p*-nitrobenzene*iso*diazotates (nitrosoamines) are formed with the greatest ease and are soluble in water, but are reprecipitated therefrom by caustic alkali. If solutions of these compounds are treated with alkaline β-naphthol, no coupling occurs for a considerable time, and the same negative result is obtained when aqueous solutions of the nitrosoamines are treated with an aqueous solution of sodium β-naphthoxide or phenoxide or of disodioresorcinol. If, however, finely powdered α- or β-naphthol, or phenol, or resorcinol, or their solutions in water, are shaken with a solution of the sodium *iso*diazotate (whether from *p*-nitroaniline, or aniline, or *p*-chloroaniline), coupling occurs rapidly and can only be due to the sequence of reactions indicated previously.

Orton (J., 1903, **83**, 796) found that in alcoholic solution Schraube and Schmidt's nitrosoamines coupled at once with sodium β-naphthoxide, owing to removal of the nitrosoamine sodium or potassium by the alcohol.

It is thus apparent why the usual coupling test failed with the *iso*diazotates, since the effect of the excess of alkali present was to retain them in the nitrosoamine form or as the *n*-diazotate ion. The coupling reaction with β-naphthol alone, indicates that the coupling reagent is the diazohydroxide in accordance with the view of Conant and Peterson (*loc. cit.*).

When a solution of β-naphthol in sodium carbonate is added to an aqueous solution of the *iso*diazotate (either from *p*-nitroaniline, aniline, or *p*-chloroaniline), coupling is delayed for several minutes, in contrast to the complete prevention of coupling which occurs when caustic alkaline solutions are used (in one experiment no coupling occurred for 3 weeks) and to the immediate coupling which occurred when the free β-naphthol was used. It was this prevention of coupling in solution of pH > 8 which led to the view that an *anti*-diazotate existed which would not couple, and on account of this negative property it was regarded as the more stable form, whereas with many of the *anti*-diazotates considerable heat is required to effect their transformation from the *syn*-form.

Bucherer and Fröhlich (*J. pr. Chem.*, 1931, **132**, 72), in a study of the action of weak acids (carbonic, boric, acetic, oxalic, and sodium bicarbonate) on the *anti*-diazotate (nitrosoamine) from *p*-nitroaniline, have concluded that the *syn*-diazotate is first formed, which is then partly hydrolysed to nitrous acid and *p*-nitroaniline, and also has its nitro-group replaced in part by hydroxyl, since the products of reaction were 4 : 4′-dinitrodiazoaminobenzene, *p*-hydroxydiazobenzene (20%), and nitrous acid. A somewhat modified mechanism would appear, however, to explain their results more simply and to avoid the assumption of an intermediate formation of *p*-nitroaniline, *viz*, that the unstable free nitrosoamine first liberated will begin to isomerise to an equilibrium mixture of the diazo- and the diazonium hydroxide, the diazohydroxide then coupling with unchanged nitrosoamine to form the 4 : 4′-dinitrodiazoaminobenzene, and the diazonium hydroxide *via* a two-point attack by water giving the *p*-hydroxydiazobenzene as follows :



An aqueous solution of the sodium nitrosoamine from *p*-nitroaniline slowly decomposes with evolution of nitrogen to form complex mixtures containing azo-phenolic compounds.

The Analogy with the Oximes.—Hantzsch reared the whole of his theory on the fundamental proposition that the difference between the oximes and the diazo-compounds lies merely in the substitution of nitrogen for carbon, and that the series of normal and *iso*diazo-compounds must in consequence be derived from the stereoisomeric diazohydroxides. Modern electronic theory was of course unknown in Hantzsch's period of activity, although he was still alive when the theory had attained considerable importance, but had passed away before the theory of resonance was developed by Pauling. On these theories, the electrons on the carbon atoms in the oxime are all employed in covalencies, whereas there is a lone pair in the corresponding nitrogen atom of the diazo-compound, which fact alone renders invalid the Hantzsch stereochemical analogy. Even if the diazohydroxides could be prepared, they could not exist in rigid structures like the oximes, since there would be easy resonance with all its consequences.

Conclusions.—(1) Hantzsch's stereo-formulation of the diazotates will not explain : (*a*) The endothermic character of the *iso*(*anti*)-forms from diazotised aniline, *o*- and *p*-toluidines, and the contrasting ready formation in the cold from diazotised *p*-nitroaniline.

(*b*) The non-existence of stereoisomeric diazo-ethers.

(*c*) The reaction of the *syn*-form with sodium stannite, and the stability of the *anti*-form towards this reagent (Hantzsch and Voch, *Ber.*, 1903, **36**, 2065).

(*d*) The fact that the *cis*(*syn*)-compound is the stronger of the *cis*- and *trans*-cinnamic acids and of the *cis*- and *trans*-benzaldoximes, whereas the opposite is the case with the hypothetical *syn*- and *anti*-diazohydroxides, known only in their salts.

(*e*) Coloured *anti*- and colourless *syn*-diazotates.

(*f*) The rapid coupling of the *syn*- and the non-coupling of the *anti*-diazotates, since it is an N—O link which must be broken in each case.

(*g*) The ephemeral existence of hydrogen compounds of the *iso*diazotates, and the formation of anhydrides from *n*-diazotates by the action of acids.

(2) Euler's view (*Ber.*, 1903, **36**, 2503, 3835) that alkaline hydrolysis of the diazo-ethers gives the *n*-diazotates is correct, since only the *n*-diazotates couple readily in the presence of alkali.

(3) All the above difficulties are removed when the *n*-diazotate is formulated as $Ar{\cdot}N{=}N{\cdot}ONa,K$, where the metal has partial ionic structure and is readily hydrolysed, and the *iso*diazotate is regarded as an ion-pair with the nitrosoamine structure. Hydrolysis of the *n*-diazotate gives the coupling reagent, $Ar{\cdot}N{=}N{\cdot}OH$, which is also liberated from the nitrosoamine by such weak acids as phenol, resorcinol, and β-naphthol. Moreover, the solid *n*-diazotates usually have water of crystallisation which may be ascribed to their partial ionic structure, the alkali metal being hydrated, whereas the *iso*diazotates crystallise with less water or none owing to the much stronger electrostatic attraction between the ions of the ion-pair. This formulation explains why sodium stannite reduces the *n*-diazotates to hydrocarbons but does not attack the *iso*diazotates, since in alkaline solution the *n*-diazotate will hydrolyse into an equilibrium mixture of the diazonium and the diazohydroxides, the former of which will be reduced by the stannite. On the other hand, an ion-pair will be preserved in the alkaline solution (cf. Saunders, *op. cit.*, p. 86) and so resist attack by the stannite.

(4) Angeli's formula, $Ar{\cdot}\overset{\displaystyle O}{\overset{\downarrow}{N}}{\cdot}N{-}$, for the *n*-diazotate ion requires facile migration of the oxygen from the nitrogen in both directions according to circumstances, and this is highly improbable; further, all the reactions for the Angeli-formulated compound require much more complicated representation than would seem to be warranted. The conversions of the azoxycarbonamides and azoxysulphones (Farrar and Gulland, *loc. cit.*) into diazo-compounds can be explained by a simple hydrolytic mechanism.

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57. *The Structure of Polyisoprenes. Part IV. Double Bond Interaction in Certain Carbalkoxy-substituted* 1 : 5-*Dienes.*

By L. BATEMAN and G. A. JEFFREY.

A peculiar lack of olefinic reactivity, combined with a facility for cyclisation of methyl and ethyl $\Delta^{1:5}$-hexadiene-1 : 1 : 3 : 3 : 4 : 4 : 6 : 6-octacarboxylates, has been attributed by Ingold, Parekh, and Shoppee to ring-chain mesomerism. A reinvestigation of these and related compounds has now been made by using *X*-ray methods, and it is shown that the crystal structure of the methyl ester is incompatible with the *cis*-configuration required for such interspatial double-bond saturation. A radical disruption of a mesomeric system by crystallisation from solution is improbable and, an earlier formulation incorporating a *bicyclo*butane nucleus being rejected on chemical grounds, it is necessary to seek a new interpretation of the anomalous reactivity. We suggest that the determinative condition is hyperconjugation throughout the carbon framework of the molecule, and discuss this in relation to 1 : 5-dienes generally.

WHEN unsaturated groups are components of a conjugated system it is well known that their individual properties are modified. Quantum mechanics now provides a sound theoretical basis for the extensive factual knowledge and even permits semi-quantitative treatment of the simpler examples (Lennard-Jones and Coulson, *Trans. Faraday Soc.*, 1939, **35**, 811). Much less understood and well defined are electronic interactions of more widely separated unsaturated centres and those in which formally saturated atoms or groups participate.

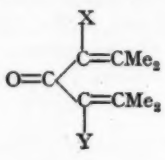
The latter type has featured prominently in the development of organic theory and is identified with two modes of electronic polarisation, *viz.*, the inductive effect, having its origin in electrostatic forces, and the tautomeric effect, resulting from a tendency to covalency change. As data have accumulated, so the complexity of electron response to environmental demand has become increasingly evident, and this is exemplified in the recognition of hyperconjugation. For some years the co-existence of the two effects acting oppositely has been assumed (*e.g.*, the $-I+T$ character of the halogens $\overset{\curvearrowleft}{\rightarrow}Cl$; Ingold, *Chem. Reviews*, 1934, **15**, 225) and a similar concept has recently been extended to the typically saturated alkyl groups (Baker and Nathan, J., 1935, 1844; Hughes, Ingold, and Taher, J., 1940, 949; Hughes and Ingold, *Trans. Faraday Soc.*, 1941, **37**, 657; Baker and Hemming, J., 1942, 191). Here, in addition to the commonly displayed inductive response, a tautomeric electron release is assigned to C–H bonds and this conjugation of unsaturated centres with saturated bond electrons—hyperconjugation (Mulliken, Riecke, and Brown, *J. Amer. Chem. Soc.*, 1941, **63**, 41)—is thought to be of wide generality. Fundamentally, the reason for the presence of different polarisations in any one group remains enigmatical, although the respective operative conditions can often be well defined (Hughes and Ingold, *loc. cit.*).

The related problem of double-bond interaction in non-conjugated dienes, which is the theme of this and the following paper, has evoked relatively negligible interest.

Müller (*Ber.*, 1921, **54**, 1466) postulated neutralisation of ethylenic activity across space to account for his

observation, which Savard (*Bull. Soc. chim.*, **1929**, **45**, 398) claims to have confirmed, that geraniol is more transparent to ultra-violet light than the corresponding mono-olefin, citronellol. This evidence must be accepted with reserve, however, in view of the well-known difficulty in obtaining pure homogeneous terpenes and their susceptibility to oxidation. A similar condition has been envisaged in certain allylic ketones showing abnormal spectra (Ramart-Lucas, Grignard's " Traité de Chimie Organique," **1936**, II, p. 86) and in support is quoted loss of ketonic function on oxime formation—a doubtful criterion, since this reaction is known to be sensitive to less specific structural changes. The absence of correlation with more general theoretical principles obviates further consideration of these ideas, but it is of interest to note the presumed diagnostic value of absorption spectra for mutual double bond saturation (cf. this vol., p. 216).

Much more significant is the work of Ingold and Shoppee who generalised their conclusions in the theory of ring-chain mesomerism. The attention of these authors (J., 1928, 365) was attracted by the pronounced change in physical and chemical properties in the series phorone, dibromophorone, bromohydroxyphorone (I, X = Y = H; X = Y = Br; X = Br, Y = OH, respectively). Colour, refractivity, and parachor all decrease markedly, and chemical reactivity parallels the increasing saturation thus revealed. A comprehensive



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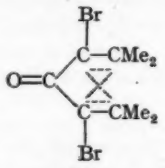

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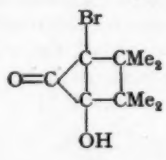


(III.)

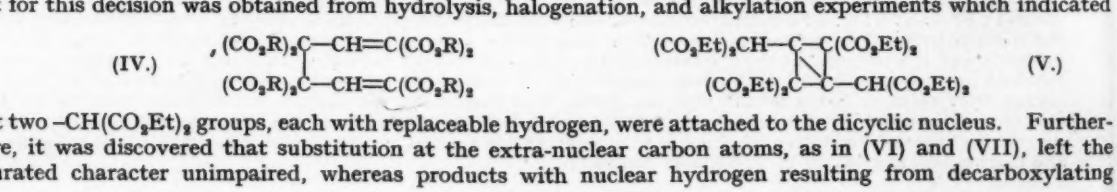
investigation indicated that, while bromohydroxyphorone is the saturated dicyclic compound (III), dibromophorone possesses hybrid character and cannot be formulated simply. The state was represented by (II), where two electrons from each double bond are shared over the dotted tracks and thereby effect a degree of bonding across space. In spite of consistent inter-relationships, such as the correlation of the electronic nature of X and Y with the position of the derivative along the (I)→(III) scale, Ingold and Shoppee appreciated the limitations of conclusions derived from these highly tautomeric systems.

The problem was therefore pursued with a series of compounds first isolated by Guthzeit and Hartmann (*J. pr. Chem.*, **1910**, **81**, 329). Reaction of sodio-dicarbethoxyglutaconic ester with iodine, and similar condensations gave a crystalline solid whose analysis and preparation were consistent with the expected product (IV, R = Et). However, the compound was remarkably resistant to the usual olefinic reagents and Guthzeit and Hartmann concluded that they had actually synthesised the *bicyclo*butane derivative (V). Support for this decision was obtained from hydrolysis, halogenation, and alkylation experiments which indicated

(IV.)

(V.)

that two $-CH(CO_2Et)_2$ groups, each with replaceable hydrogen, were attached to the dicyclic nucleus. Furthermore, it was discovered that substitution at the extra-nuclear carbon atoms, as in (VI) and (VII), left the saturated character unimpaired, whereas products with nuclear hydrogen resulting from decarboxylating



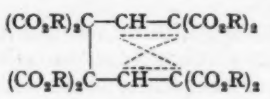
(VIII.) (VII.)

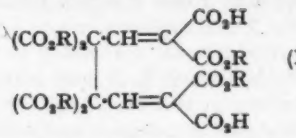
hydrolysis readily reduced permanganate—the inference being that such replacement afforded the means for disruptive nuclear attack.

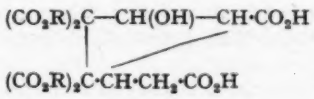
In their re-investigation, which included the corresponding methyl analogues, Ingold, Parekh, and Shoppee (J., **1936**, 142) confirmed that the octa-esters had all the reputed stability towards permanganate but found equal resistance to halogenation and alkylation. Hydrolytic degradation proceeded in the stages described, but the decarboxylated derivatives all contained a combined molecule of water additional to the reported composition, and the alleged unsaturation of certain acids, *e.g.*, that formulated as (VIII), proved to be fictitious. Because of these discrepancies and to explain ozonolyses, realised with difficulty, in which the octa-esters underwent scission in agreement with formula (IV), the bicyclic formula (V) was rejected in favour of (IX) with resonance interaction of the double bonds, precisely as in dibromophorone.* The hexa-ester diacid

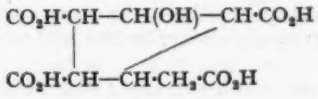
* The only other compounds based on the *bicyclo*butane ring system are described by Beesley and Thorpe, J., 1920, **117**, 591.

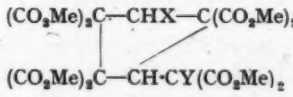
(*ex* VI) was reformulated as (X, R = Et) with similar mesomerism, but the acids supposedly (VII) and (VIII) correspond to the *cyclo*pentane derivatives (XI) and (XII). Slight, but significant differences appeared in the

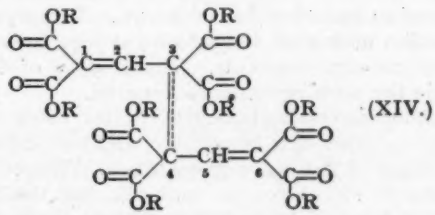
(IX.) 


(X.)

(XI.) 


(XII.)

(XIII.) 


(XIV.)

methyl series. Dissolution of the octamethyl ester in cold dilute methyl-alcoholic sodium methoxide and subsequent acidification gave, not the hexa-ester diacid (X, R = Me) as in the ethyl series, but a compound of the ester and methyl alcohol (XIII, X = OMe, Y = H). This distilled without decomposition, in common with the other neutral esters containing combined water [*e.g.*, esters of (XI) and (XII)] but in contrast to the parent ester. Finally, electrolytic reduction gave a fully saturated dihydro-derivative, which also distilled unchanged and whose formulation as (XIII, X = Y = H) was further supported by relating its complete hydrolytic degradation product to the acid (XII).

The reactivity of the octa-esters is clearly paradoxical. On the one hand, the ethylenic bonds revealed by ozonolysis are highly resistant to the usual addenda; on the other, *one* molecule of a normally less active reagent combines easily under acid or alkaline conditions with concomitant cyclisation. The double bonds appear to be interconnected in some way, and Ingold, Parekh, and Shoppee identified this with the resonance electron exchange depicted in (IX).

The possibility of an alternative explanation was suggested by a complete *X*-ray structure analysis of the typical straight chain polyisoprene derivative, geranylamine hydrochloride (Jeffrey, *Proc. Roy. Soc.*, in the press; see Bateman and Jeffrey, *Nature*, **1943**, **152**, 446), in which the central C–C bond of the 1 : 5-diene system formed by *trans*-linked isoprene units was found to be abnormally short. This feature is commonly associated with single bonds bounded by conjugated unsaturated centres, and although it is not entirely unexpected theoretically (Bateman, *Trans. Faraday Soc.*, **1942**, **38**, 367) yet the reason for its existence in a 1 : 5-diene remains obscure. A tentative explanation (Bateman and Jeffrey, *loc. cit.*) in terms of hyperconjugation has yet to receive experimental support and in simple systems this presents some difficulty.

Now the double bonds in the octa-esters are also 1 : 5-spaced, and it is reasonable to enquire whether their peculiar properties originate in similar but more extensive chain hyperconjugation. Superficial resemblances are at once apparent; cyclisation following the addition of one molecule of reagent is common to the acid hydration and other reactions (Bloomfield, J., **1943**, 289; **1944**, 114) of open-chain terpenes, and the relatively easy thermal breakdown at the central C–C bond (Ingold and Shoppee, J., 1930, 1619; Ingold, Parekh, and Shoppee, *loc. cit.*) suggests facilitation by allylic resonance energy (Huckel, *Z. Elektrochem.*, **1937**, **43**, 841).

When the octa-ester is written as (XIV) the molecule is seen to possess high latent conjugation whose development is a function of the electron-conducting capacity of the central C–C bond. Full conjugation will create a system of much lower energy, and the tendency to approach this state will be a driving force offsetting the barriers imposed by single-bond insulation and by normal orbital hybridisation, as is true indeed of any mesomeric system. Although the octa-esters differ from relevant hydrocarbons by the absence of hydrogen at carbon atoms 3 and 4 (XIV), yet Hughes and Ingold (*loc. cit.*; Hughes, Ingold, Masterman, and McNulty, J., 1940, 899) have stressed that all quasi-unsaturated groups have hyperconjugative powers and this will certainly be true of the highly polarisable carbalkoxyl groups. It may be noted that the carbon atoms forming the central bond are flanked by atoms contributing sp^2 bonding orbitals. Hence symmetrical sp^2 hybridisation at the former may not be energetically favoured, but instead a characteristic hybridisation in which the hybrid bond has an added measure of electronic transmission over that of a normal single bond (possibly lower s/p ratio). In this sense, a normal double bond is simulated, but the absence of π electrons in the hybrid bond limits further similarity (*e.g.*, lack of additive function and ultra-violet absorption differences—Bateman and Koch, J., 1944, 600). It is perhaps significant that the octa-esters are labile under conditions of electrical asymmetry where transmissive powers will be invoked to the full.

The consequence of chain hyperconjugation to molecular structure cannot be definitely predicted. In normal conjugation, a *trans*-planar configuration is usual owing to enhancement of the resonance process, and

a similar orientation about the hybrid bond, as in geranylamine hydrochloride, might well be anticipated in the octa-esters. Ring-chain mesomerism, on the other hand, necessarily requires a *cis*-arrangement. A discrimination between these theories becomes possible therefore by configuration analysis, and we have undertaken this by *X*-ray methods.

In general, intramolecular symmetry is not revealed by *X*-rays without recourse to a complete crystal structure analysis, but when it is used in symmetry operations effecting translations in the crystal lattice, systematic extinctions occur in the diffraction pattern that permit recognition from readily accessible data. A centre of symmetry can be unequivocally identified providing that the compound crystallise in a particular lattice arrangement and that its molecular complexity be known from an independent source. In practice, the latter condition can nearly always be met, and the success of the method essentially depends on Nature providing the former.

The octaethyl ester was examined first for symmetry character and proved to be an example from which no certain conclusion can be drawn. The crystals are triclinic with one molecule in the unit cell, and *X*-ray diffraction makes no distinction between the space group $P1$, with an asymmetric molecule, and $P\bar{1}$, with a centrosymmetric molecule. The absence of detectable pyroelectric effect indicates the latter but does not provide the decisive evidence required.

The corresponding octamethyl ester, however, showed the presence of a centre of symmetry unambiguously. The crystal system is monoclinic, and very careful indexing of oscillation photographs revealed the systematic extinctions of the space-group $P2_1/a$. The combination of two-fold screw axis and glide plane requires four asymmetric structures per unit cell, but the observed density limits the number of molecules to two, and hence each molecule must provide two centrosymmetrically related units. A *cis*-configuration is impossible, and ring-chain mesomerism must be rejected as a structural feature of the crystalline state.

In addition to this approach, the unit cells of some derivatives and related compounds were measured in the hope that decisions between *cis*-, *trans*-, and cyclic structures might be made from a study of intermolecular packing. No systematic variations in molecular dimensions could be traced, and inspection of Stuart models makes it plain that the presence of several carbalkoxyl groups, each with some freedom of orientation, swamps the slight differences introduced by rearrangement of the central carbon framework. For example, the symmetrical *trans*-forms of the uncyclised esters fitted the unit cells excellently, but the *cis*- and dicyclic forms were not sufficiently different to make them inadmissible. At the same time, Ingold, Parekh, and Shoppee's experimental record, where repeated, was confirmed in all essential respects, both chemically and by *X*-ray molecular-weight determinations. We also identified three forms of the hexamethyl ester diacid (X, R = Me), one containing acetone of crystallisation, and two forms of the acid esters (XI, R = Me and Et, respectively), one hydrated in each case. *X*-Ray data are given for crystalline methyl $\alpha\gamma$-dicarbomethoxyglutaconate, for its

(XV.) $(CO_2Et)_2C(Et)-CH=C(CO_2Et)_2$ $\qquad$ $(CO_2R)_2C(-CH\cdot CH(CO_2R)_2)-CH(CO_2R)\cdot CH-C(CO_2R)_2$ (XVI.)

*cyclo*butane *dimer* (XVI, R = Me), which proved to be centrosymmetric, and for the two stereoisomeric *dimers* (XVI, R = Et) of ethyl $\alpha\gamma$-dicarbethoxyglutaconate. The configurations adduced for the latter on chemical grounds (Ingold, Perren, and Thorpe, J., 1922, 1765) are supported but not conclusively proved.

The non-existence of ring-chain mesomerism in the crystal raises the question whether this is also true in the liquid phase where the anomalous reactivity is observed. Intramolecular association of the double bonds is considered to induce a state of lower energy owing to the greater freedom of the electrons than when confined to normal bonds. If such a preferred state does exist in solution, a configurational change to the *trans*-structure on crystallisation is possible only if accompanied by similar but intermolecular mesomerism and by improved crystal packing. We see no reason to expect special crystal forces and, in fact, the simple unit cells of the octa-esters, in contrast to the acid esters (XI, R = Me or Et), and particularly their hydrates, where hydrogen bonding is a structural condition, are indicative of nothing more than ordinary van der Waals attractions. The direct examination of the molecular state in solution described in the accompanying paper supports this reasoning.

The *X*-ray data are only compatible with formula (V) if the carbon nucleus is assumed to be planar. This is highly improbable stereochemically, and the rejection of the *bicyclo*-structure on chemical and spectral evidence (this vol., p. 217) is therefore confirmed.

There is then no alternative but to accept the open-chain formula and to seek another explanation of the unusual chemistry. Depression of double-bond activity may be due to the deactivating carbalkoxyl substituents or to steric hindrance. Ethyl $\alpha\gamma$-dicarbethoxy-α-ethylglutaconate (XV), where the double bond has the same group environment, is also resistant to additive reagents. Comparative experiments show that it reduces potassium permanganate in acetone solution roughly 15 times as rapidly as the octaethyl ester at the same molar concentration. Although this rate difference, which is half the true comparative value if the double bond is the seat of oxidative attack and if the rate is directly proportional to olefin concentration, might be attributed to the heavier side-chain substitution in the octa-ester, present knowledge indicates that this interpretation is probably inadequate. Although other substituted glutaconic acids show normal, if greatly reduced, olefinic activity (*e.g.*, $\alpha\alpha\beta$-trimethyl-, Perkin and Thorpe, J., 1897, **71**, 1182; $\alpha\alpha\gamma$-trimethyl-, Blaise, *Compt. rend.*, 1903, **136**, 1141; Perkin and Smith, J., 1903, **83**, 777), yet Ingold, Parekh, and Shoppee (*loc. cit.*) have isolated the hexa-ester diacid from the action of permanganate on the octamethyl ester, a result which recalls

the inertness of the double bond and the lability of the alkyl group in tetraethylethane towards the same reagent (Koch and Hilberath, *Ber.*, 1940, **73**, 1171). Unless it can be shown, contrary to these indications of more profound reactivity difference, that the measured oxidation is initiated at the double bond in both cases, rate comparison has little value. Nevertheless, we think that the common substitutional influences must be reckoned with in assessing additive function in these systems.

Of greater significance is the cyclisation propensity. This is characterised by simultaneous addition of a molecule A–B such that A adds to one olefinic centre, B to the other—a feature clearly similar to 1 : 4-addition to butadiene except that valency redistribution occurs through internal bonding instead of by double-bond shift. As Ingold *et al.* argued, acceptance of partial double-bond interaction seems inevitable, and we suggest that this has now to be identified with chain hyperconjugation. In effect, this result generalises a principle familiar in the aromatic series (*e.g.*, the benzenoid character of pyrrole, furan, and thiophen and perhaps of *cyclo*hexadiene, cf. Bateman and Koch, *loc. cit.*; and the ionicity of the CH_2 group in the series *cyclo*pentadiene, indene, fluorene), *viz.*, that the intervention of a saturated group does not entirely thwart the development of full molecular conjugation.

Experimental.

No original preparations were undertaken, but certain differences were found from the m. p. data of Ingold, Parekh, and Shoppee, whose values are therefore given in parentheses for comparison. The density units are g./c.c.

Methyl αγ-dicarbomethoxyglutaconate. M. p. 50—51° (43°; cf. this vol., p. 221). Large triclinic crystals tabular on (100) with cell dimensions $a = 12{\cdot}26$, $b = 8{\cdot}79$, $c = 8{\cdot}30$ A., $\alpha = 115°$, $\beta = 115°$, $\gamma = 113°$; $V = 666$ A.^{3}. Hence, with 2 molecules in the cell, the observed density of 1·38 gives M, 277 (Calc.: 274).

Octamethyl ester. M. p. 141° (139°) (Found: C, 48·35; H, 4·85; M, by vapour-pressure equilibration of a benzene solution against olive oil, 540 ± 30; cryoscopically in benzene, 530 ± 30. Calc. for $C_{22}H_{34}O_{16}$: C, 48·35; H, 4·8%; M, 546). Crystallises from acetone and a little light petroleum (b. p. 60—80°) in monoclinic prisms with forms {010}, {001}, {110}. Cell dimensions: $a = 10{\cdot}39$, $b = 14{\cdot}60$, $c = 8{\cdot}37$ A., $\beta = 103{\cdot}5°$; $V = 1234$ A.^{3}. Very careful indexing of oscillation photographs revealed systematic extinctions of $(0k0)$ absent for k odd, and $(h0l)$ absent for h odd with no exceptions. The space-group is therefore $P2_1/a$, requiring 4 asymmetric structure units. The observed density is 1·48 and that calculated for 2 centrosymmetric molecules in the cell is 1·47.

Octaethyl ester. M. p. 86° (Found: C, 54·7; H, 6·45. Calc. for $C_{30}H_{46}O_{16}$: C, 54·7; H, 6·45%). Triclinic crystals with {100}, {102}, {001}, {010}, commonly developed, also occasionally {011} and {101}. Cell dimensions: $a = 12{\cdot}24$, $b = 8{\cdot}72$, $c = 8{\cdot}72$ A., $\alpha = 97{\cdot}5°$, $\beta = 104{\cdot}5°$, $\gamma = 107{\cdot}5°$; $V = 855$ A.^{3}. Absence of pyroelectric effect indicates a space group $P\bar{1}$ with one centrosymmetric molecule. d(obs.) = 1·275, whence $M = 657$ (Calc.: 658).

Comparative Reducing Power of the Octaethyl Ester and Ethyl αγ-Dicarbethoxy-α-ethylglutaconate towards Permanganate.—Attempts to measure the reduction in acetone solution quantitatively by an absorptionmeter were abandoned, partly owing to the development of a brownish tinge as the pink colour faded, with subsequent coagulation of the manganese dioxide, and partly because the octa-ester invariably gave an opaque solution as reaction proceeded. Instead, a deficit of permanganate was used and the time for complete disappearance of colour measured. A trace of acid was added to eliminate adventitious variations due to possible sensitivity to pH conditions (*e.g.*, induction period). In the absence of thermostatic temperature control (2° range) the solutions were maintained under the same conditions throughout the whole of the reaction. A typical experiment was: Solution A: octa-ester, 0·0213M; $KMnO_4$, 0·00052M; HCl, 0·00003N. Solution B: ethylated tetra-ester (p. 214), 0·0215M; $KMnO_4$ and HCl as in A. Solution C: $KMnO_4$ and HCl as in A. A was decolourised in 52 hours, B in 4 hours, and C had faded slightly in 52 hours. Three similar experiments gave a mean reduction time ratio for A/B of 15±4.

Hexamethyl Ester Diacid (X, R = Me).—Difficulty was experienced in obtaining suitable crystals for *X*-ray work, and crystallisation behaviour was capricious generally. Two apparently isomorphous and visually indistinguishable forms were isolated from acetone: an anhydrous form (1), and an unstable solvated form (2) which lost solvent on standing in air. The former was usually obtained, the latter rarely, and the conditions favouring the formation of either crystals were not discovered. Form (1) had m. p. 225—226° (decomp.) (218°) (Found: C, 46·3; H, 4·5. Calc. for $C_{20}H_{22}O_{16}$: C, 46·3; H, 4·3%); monoclinic plates with $a = 18{\cdot}4$, $b = 8{\cdot}55$, $c = 14{\cdot}3$ A., $\beta = 92°$; $V = 2248$ A.^{3}. The space-group is $C2/c$ with 4 centrosymmetric molecules, or Cc with 8 asymmetric molecules; d(obs.) = 1·55, whence $M = 523$ (Calc.: 518). Form (2) had the same m. p. after loss of solvent; on standing, the crystals became opaque and this change was reflected in the analytical figures (Found: after *ca.* 7 days, C, 48·7; H, 5·15; after *ca.* 10 days, C, 48·3; H, 5·0; after 24 weeks, C, 46·25; H, 4·35; equiv., by titration, 263. $C_{20}H_{22}O_{16},2C_3H_6O$ requires C, 49·2; H, 5·35%; M, 634); cell dimensions: $a = 23{\cdot}00$, $b = 8{\cdot}05$, $c = 16{\cdot}75$ A., $\beta = 93°$, $V = 3100$ A.^{3}. Space-group also $C2/c$ or Cc; d(obs.) = 1·35, whence $M = 629$. The acid was slightly soluble in hot water, the cooled solution depositing a third crystalline form (3) as very small triclinic prisms of the same m. p. (Found: C, 46·05; H, 4·4%); cell dimensions: $a = 10{\cdot}01$, $b = 8{\cdot}24$, $c = 8{\cdot}20$ A., $\alpha = 118°$, $\beta = 109°$, $\gamma = 108°$; $V = 555$ A.^{3}; $n = 1$; d(obs.) = 1·57, whence $M = 524$.

Hexaethyl Ester Diacid (X, R = Et).—M. p. 191—193° (193°). Triclinic prisms with $a = 11{\cdot}07$, $b = 8{\cdot}92$, $c = 8{\cdot}55$ A.; $\alpha = 119°$, $\beta = 106°$, $\gamma = 94°$; $V = 715$ A.^{3}. d(obs.) = 1·385, whence $M = 596$ (Calc.; 620). Absence of pyroelectric effect indicates one centrosymmetric molecule in the cell.

Hexaethyl Ester Diacid Chloride.—M. p. 66·5—67° (65—66°). Monoclinic prisms with $a = 27{\cdot}86$, $b = 8{\cdot}73$, $c = 12{\cdot}96$ A., $\beta = 98{\cdot}5°$; $V = 3117$ A.^{3}; $n = 4$; d(obs.) = 1·355, whence $M = 635$ (Calc.: 639). Space group $P2/a$.

Dihydro-octamethyl Ester (XIII, X = Y = H).—M. p. 156°, with previous softening (149°) (Found: C, 48·25; H, 5·2. Calc. for $C_{22}H_{28}O_{16}$: C, 48·2; H, 5·15%). Monoclinic prisms with $a = 19{\cdot}63$, $b = 12{\cdot}19$, $c = 11{\cdot}51$ A., $\beta = 109°$, $V = 2603$ A.^{3}; $n = 4$; d(obs.) = 1·40, whence $M = 548$ (Calc.; 548). Space-group $C2/c$.

Methyl cyclo*Pentane Hydroxy-acid Ester* (XI, R = Me).—Anhydrous (1) and hydrated (2) forms were isolated on crystallisation from water. Form (1) had m. p. 248—250°, with previous softening (245°) (Found: C, 45·8; H, 4·85. Calc. for $C_{16}H_{20}O_{13}$: C, 45·7; H, 4·8%). Orthorhombic bipyramids with $a = 26{\cdot}62$, $b = 18{\cdot}65$, $c = 16{\cdot}34$ A.; $V = 7616$ A.^{3}; $n = 16$; d(obs.) = 1·47, whence $M = 421$ (Calc.: 420). Form (2) afforded orthorhombic needles with $a = 62{\cdot}7$, $b = 26{\cdot}66$, $c = 12{\cdot}15$ A.; $V = 20310$ A.^{3}; $n = 32 + 256H_2O$; d(obs.) = 1·47, whence $M = 562$ ($C_{16}H_{20}O_{13},8H_2O$ requires M, 564).

Ethyl cyclo*Pentane Hydroxy-acid Ester* (XI, R = Et).—Again, anhydrous (1) and hydrated (2) forms were isolated. The first, crystallised from ether and ligroin, had m. p. 153—154° (152°) (Found: C, 50·4; H, 5·95. Calc. for $C_{28}H_{38}O_{13}$: C, 50·4; H, 5·9%); orthorhombic pyramids, usually penetration twins, with $a = 29{\cdot}46$, $b = 19{\cdot}45$, $c = 16{\cdot}47$ A.; $V = 9437$ A.^{3}; $n = 16$; d(obs.) = 1·345, whence $M = 478$ (Calc.: 476). The *hydrate* (2) crystallised from water (Found: C, 48·4, 48·5; H, 6·1, 6·15. $C_{28}H_{38}O_{13},H_2O$ requires C, 48·5; H, 6·1%) in monoclinic prisms with $a = 19{\cdot}08$,

$b = 15{\cdot}61$, $c = 8{\cdot}80$ A., $\beta = 112°$; $V = 2430$ A.^{3}; $n = 4$; d(obs.) = 1·32, whence $M = 483$ (Calc. : 494). Space-group $P2_1/a$. Guthzeit and Hartmann reported a trihydrate, $C_{20}H_{16}O_{12},3H_2O$, *i.e.*, $C_{20}H_{22}O_{13},2H_2O$, but, in agreement with Ingold, Parekh, and Shoppee, we failed to isolate this. The monohydrate now described is new.

Dimer of Methyl αγ-Dicarbomethoxyglutaconate (XVI, R = Me).—M. p. 222° (Found : C, 48·45; H, 5·25. $C_{22}H_{28}O_{14}$ requires C, 48·2; H, 5·15%); monoclinic prisms with $a = 11{\cdot}00$, $b = 14{\cdot}18$, $c = 8{\cdot}13$ A., $\beta = 99{\cdot}5°$; $V = 1250$ A.^{3}; $n = 2$; d(obs.) = 1·44, whence $M = 542$ (Calc. : 548). Extinctions correspond to the space-group $P2_1/n$. The molecules must therefore possess a centre of symmetry and their configuration is probably analogous to that of the corresponding ethyl dimer, m. p. 103°, as proposed by Ingold, Perren, and Thorpe (*loc. cit.*).

Dimers of Ethyl αγ-Dicarbethoxyglutaconate (XVI, R = Et).—(1) M. p. 103° (Found : C, 54·4; H, 6·7. $C_{30}H_{44}O_{16}$ requires C, 54·5; H, 6·7%); tabular triclinic crystals with $a = 11{\cdot}81$, $b = 9{\cdot}49$, $c = 9{\cdot}37$ A., $\alpha = 111°$, $\beta = 111°$, $\gamma = 112{\cdot}5°$; $V = 875$ A.^{3}; $n = 1$; d(obs.) = 1·25, whence $M = 658$ (Calc. : 660). Space-group probably $P\bar{1}$, with centro-symmetric molecule. (2) M. p. 86—87° (Found : C, 54·35; H, 6·8%); short monoclinic needles with $a = 26{\cdot}28$, $b = 12{\cdot}49$, $c = 21{\cdot}42$ A., $\beta = 101{\cdot}5°$; $V = 6890$ A.^{3}; $n = 8$; d(obs.) = 1·27, whence $M = 660$. Space group $A2/a$.

Our thanks are due to Dr. W. T. Chambers and Miss H. Rhodes for the micro-analyses and to Dr. G. Gee for the isopiestic molecular-weight determination.

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58. *The Structure of Polyisoprenes. Part V. Ultra-violet Absorption Spectra of Certain Carbalkoxy-substituted* 1 : 5-*Dienes, and the Charge-resonance Spectra of Glutaconic Ester Enolate Ions.*

By L. BATEMAN and H. P. KOCH.

Spectral evidence supports the conclusion reached in Part IV that ring-chain mesomerism in methyl and ethyl $\Delta^{1:5}$-hexadiene-1 : 1 : 3 : 3 : 4 : 4 : 6 : 6-octacarboxylates is non-existent in solution just as in the crystalline state. The data are not inconsistent with chain hyperconjugation in these molecules. The marked change in structural type that follows the addition of one molecule of hydrogen or hydrolytic reagent has been verified spectrographically.

The spectra of methyl and ethyl αγ-dicarboxyglutaconic esters and their sodium and cupric derivatives have been measured in various solvents, and tautomeric behaviour compared with that of other keto-enols. Of special interest is the intense long-wave absorption band of the enolate ions, which are recognised as simple structural analogues of the cyanine dyes giving rise to similar charge-resonance spectra. A preliminary comment is made on the present accepted structure of ethyl 6-ethoxy-α-pyrone-3 : 5-dicarboxylate.

IT was pointed out in Part IV (preceding paper) that, both in empirical hypotheses and in the electronic theory of ring-chain mesomerism, double-bond interaction across space was thought to create a more saturated molecular condition which a short-wave shift in ultra-violet absorption would serve to reflect. Thus in the phorone series (this vol., p. 212) the normally unsaturated phorone is bright yellow, dibromophorone in which ring-chain mesomerism is postulated is only faintly coloured, and the saturated dicyclic bromohydroxyphorone is colourless.* Similar ring-chain mesomerism has been attributed to the octa-esters (I, R = Me or Et) in order to explain their peculiar chemical behaviour (Ingold, Parekh, and Shoppee, J., 1936, 142), but *X*-ray examination now shows that the methyl ester and almost certainly the ethyl ester do not possess *cis*-configurations in the

(I.) $(CO_2R)_2C{=}CH{-}C(CO_2R)_2$ / $(CO_2R)_2C{-}CH{=}C(CO_2R)_2$ $\qquad$ $(CO_2R)_2C{=}CH{-}C(CO_2R)_2$ (II.) / X

crystalline state. Interspatial double-bond saturation is thus invalidated, but only by indirect arguments was it possible to extend the conclusion to conditions where the anomalous reactivity is actually observed. Spectrographic data were therefore required for two main reasons : (i) ring-chain mesomerism analogous to that envisaged in dibromophorone demands similar spectral consequences, and (ii) the molecular state in solution is directly investigated. In addition, the purity of preparative intermediates could be checked and it has been possible to confirm the basic structure assigned to certain derivatives.

The spectrographic approach is essentially a comparison of the octa-esters with a chemically normal analogue (II). However, of intrinsic interest to tautomeric and spectral theory is the rather complex spectroscopic and chemical behaviour of the αγ-dicarbalkoxyglutaconic esters (II, X = H) and this is discussed separately in the second part of this paper.

Spectrographic Examination of the Octa-esters (I), Some Derivatives, and Related Compounds.—The ultra-violet absorption of the octaethyl ester (I, R = Et) had been examined qualitatively by Hartmann (*J. pr. Chem.*, 1911, **83**, 190) and adduced in support of the original bi*cyclo*butane formulation (cf. this vol., p. 212)—a conclusion definitely inacceptable in the light of the present work. Measurements in alcoholic solution of the octa-ethyl and -methyl esters, together with those of ethyl αγ-dicarbethoxy-α-ethyl glutaconate (II, R = X = Et), are recorded in Fig. 1, where ε is plotted per tetra-ester residue. The absorption of all these compounds is very similar to that exhibited by the parent tetra-ester (II, R = Et, X = H) in hexane or acidified alcohol (see p. 217) and is typical of the normal $C{=}C{-}CO_2R$ chromophore, *e.g.*, crotonic acid,

* Excluding the doubtful data of Müller and of Savard (cf. this vol., p. 211), it may be noted that the carbonyl chromophore is involved in all absorption anomalies of this type.

$CH_3 \cdot CH{:}CH \cdot CO_2H$, has $\lambda_{max.}$ 2040 A., $\varepsilon = 12{,}000$ in alcohol (Hausser, Kuhn, *et al.*, *Z. physikal. Chem.*, 1935, *B*, **29**, 371). The absorption processes at the double bonds in the octa- and tetra-esters are evidently the same and, of special importance to the present problem, no absorption shift is apparent which is remotely comparable with that from phorone to dibromophorone. Support is thus derived for the arguments presented in the preceding paper that the non-existence of ring-chain mesomerism in the crystal applies equally to the dissolved state. Moreover, the correctness of the bi*cyclo*butane formula is rendered still less probable since conjugation of carbalkoxyl groups with a saturated, if strained, carbon nucleus would certainly be characterised by a distinct and less absorptive spectrum, as is the comparable *cyclo*propane conjugation (Carr and Burt, *J. Amer. Chem. Soc.*, 1918, **40**, 1590; Klotz, *ibid.*, 1944, **66**, 88).

The evidence was surveyed in Part IV which led Ingold, Parekh, and Shoppee to formulate the hexa-ester diacid derivatives as structural analogues of the octa-esters but, in contradiction to Guthzeit and Hartmann, to recognise a profound structural change on hydrolytic degradation. The absorption of the hexamethyl ester diacid can be compared in Fig. 1 with that of the acid-ester degradation product, the dihydro-octamethyl ester, and the octamethyl ester–methyl alcohol compound, three substances which, according to Ingold *et al.*, are related *cyclo*pentane derivatives. The large spectral difference fully supports the proposed change in

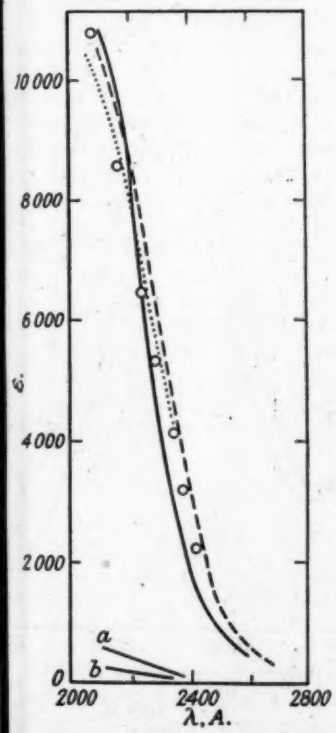


FIG. 1.

Spectra in ethyl-alcoholic solution.

———— *Ethyl αγ-dicarbethoxy-α-ethylglutaconate.*
— — — — *Octaethyl ester.*
..... *Octamethyl ester.*
○ ○ ○ *Hexamethyl ester di-acid.*
a *Ethyl* cyclo*butane octa-ester; dihydro-octamethyl ester; octamethyl ester–methyl alcohol compound.*
b *Hydrolytic degradation product (tetramethyl ester diacid) (ε per half-molecule).*

structural type and, indeed, comparison with the saturated *cyclo*butane dimer of ethyl dicarbethoxyglutaconate (Fig. 1) and consideration of the actual intensity values leave no doubt that the structural change is from molecules with two double bonds, each conjugated with carbalkoxyl groups, to non-olefinic carbalkoxy-compounds.

Normal substitutional influences seem inadequate to account for the chemical peculiarities of the octa-esters, and it has been suggested that the unique molecular condition is determined by chain hyperconjugation (this vol., p 213). It has already been shown (Bateman and Koch, J., 1944, 600) that the marked bond shortening in geranylamine hydrochloride, also attributed to chain hyperconjugation in 1 : 5-dienes, is not detectable by absorption in the quartz ultra-violet region. A similar interpretation of the chemistry of the octa-esters is compatible therefore with the spectral evidence, although its non-specificity precludes its use in a confirmatory sense.

Spectra and Tautomerism of Glutaconic Acid Derivatives.—Stobbe and Wildensee (*J. pr. Chem.*, 1927, **115**, 163) studied the tautomeric behaviour in various solvents of ethyl αγ-dicarbethoxyglutaconate (II, R = Et, X = H) spectrographically, by the Hartley–Baly method, and by rough colorimetry with ferric chloride. The enol form, fully characterised by the sodio-derivative (X = Na), exhibited intense selective absorption at *ca.* 2600 A. and especially at *ca.* 3600 A., and these bands also appeared, though much more feebly, when the parent ester was dissolved in neutral ethyl alcohol. The alcoholic solution, however, did not obey Beer's law and the increased absorption intensity observed on dilution was recognised as a measure of increasing enol content. In ether, chloroform, hexane, or acidified alcohol, only fairly strong end absorption occurred, and

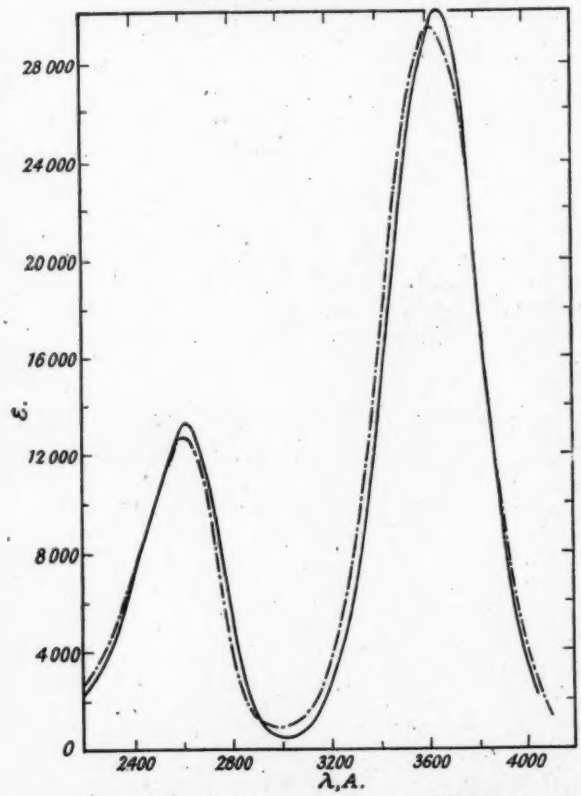
if the α-carbon atom was ethylated (X = Et) similar but slightly greater end absorption resulted in either neutral or acidified alcohol or in hexane.

Our measurements on the pale yellow sodio-derivatives of the methyl and ethyl tetra-esters (II, X = Na, R = Me or Et) in ethyl-alcoholic solution are shown in Fig. 2. The corresponding green cupric derivatives have similar spectra in the ultra-violet (Fig. 3), but Beer's law is not obeyed. The absorption bands are displaced and less intense, but the curves suggest that at infinite dilution the spectra of the sodio-compounds will be exactly reproduced.

Neutral alcoholic solutions of the parent tetra-esters show the long-wave band of the respective sodio-derivatives at precisely the same wave-lengths, and the other band, although obscured by end absorption at the higher concentrations, is indicated by the inflection in the curves obtained from the more dilute solutions (Fig. 4). The intensity of these bands increases markedly on dilution, and if we assume that the pure enol

FIG. 2.

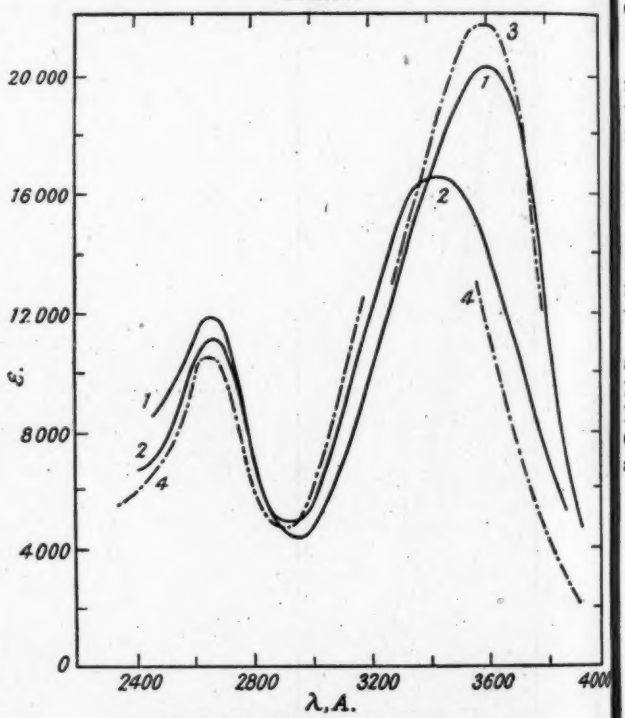
Sodio-derivatives of dicarbethoxyglutaconic esters in ethyl-alcoholic solution.



——— *Ethyl ester.* —·—·—·— *Methyl ester.*

FIG. 3.

Copper salts of dicarbalkoxyglutaconic esters in ethyl-alcoholic solution.



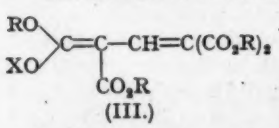
1. *Ethyl ester*, $[Cu^{++}] = 10^{-4}$ M.
2. ,, ,, ,, $= 5{\cdot}2 \times 10^{-4}$ M.
3. *Methyl* ,, ,, $= 3 \times 10^{-5}$ M.
4. ,, ,, ,, $= 7{\cdot}5 \times 10^{-4}$ M.

form of the ester has the same absorption intensity as the sodio-compound, the equilibrium concentration of enol at the dilutions studied is readily calculated.

Ester.	Concn., M.	Intensity, ε.	Enol, %.
Tetramethyl	0·0103	170 ($\lambda_{max.}$ = 3630 A.)	0·6
,, ...	0·0004	3250	11
Tetraethyl	0·0125	135 ($\lambda_{max.}$ = 3660 A.)	0·4$_5$
,, ...	0·0005	2350	8

In acidified alcohol, selective absorption disappears entirely (Fig. 4), and only end absorption corresponding to the C=C—CO_2R chromophore is observed.

The classical enol formula (III, X = H) is inadequate to account for this varied behaviour, and the following points call for comment: (i) The free esters in neutral alcohol and their sodio-derivatives exhibit the same near ultra-violet absorption bands; (ii) the main enol band occurs at remarkably long wave-lengths; (iii) solutions of the copper derivatives show the enol bands displaced and of reduced intensity, but the full intensity at the usual wave-lengths is apparently developed at infinite dilution; (iv) solvent effects on the keto-enol equilibrium.



(III.)

(i) The first point implies that the hydrogen enol and its salt have the same electronic structure, in contrast to the enols of ketones such as ethyl acetoacetate, acetylacetone, etc., whose ionic salts always absorb more or less differently (at longer wave-lengths) and where it has been inferred that the salts possess somewhat different types of bonding (Hantzsch, *Ber.*, 1910, **43**, 3058; Morton, Hassan, and Calloway, J., 1934, 883).

(ii) The structural factors governing the wave-length position of the first strong absorption band of conjugated compounds are now fairly well understood, mainly owing to the experimental work of Hausser and Kuhn on polyenes (*Z. physikal. Chem.*, 1935, *B*, **29**, 363, and following papers), and of Brooker on cyanine dyestuffs (*Rev. Mod. Physics*, 1942, **14**, 275).

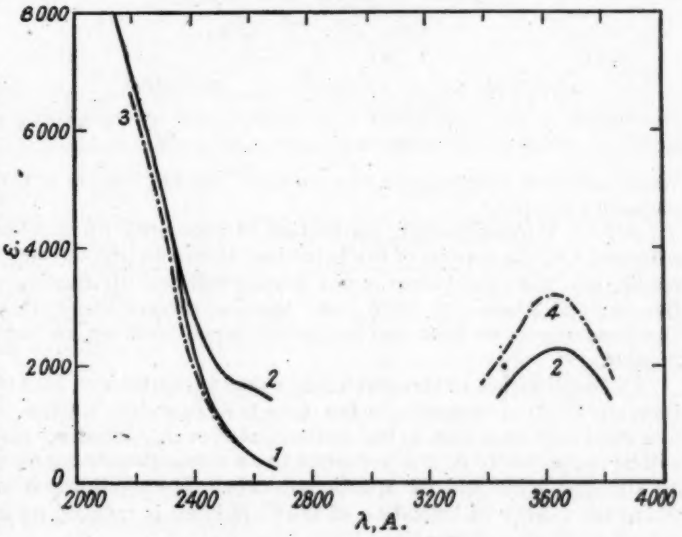
Hausser and Kuhn and their collaborators found that the position of maximum absorption shifts to longer wave-lengths as n increases in the series A—$[CH{=}CH]_n$—B. In practice, absorption spectra of natural and synthetic polyenes of this type have often been employed as structural criteria since a reliable value of n can usually be deduced from $\lambda_{max.}$. The degree of conjugation present in the enol formulation (III) is similar to that of sorbic or muconic acid,

$CH_3{\cdot}[CH{=}CH]_2{\cdot}CO_2H$

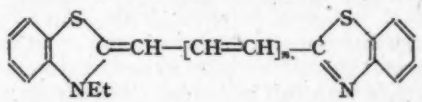
and $CO_2H{\cdot}[CH{=}CH]_2{\cdot}CO_2H$, which have $\lambda_{max.}$ 2540 and 2630 A., respectively (Hausser, Kuhn, *et al.*, *loc. cit.*, pp. 372, 383). Absorption beyond 3600 A. is not in fact observed until the homologue $CH_3{\cdot}[CH{=}CH]_5{\cdot}CO_2H$ is reached (*ibid.*, p. 403), so it is obvious that a structural condition other than, or additional to, ordinary conjugation is operative in the enols of the tetra-esters.

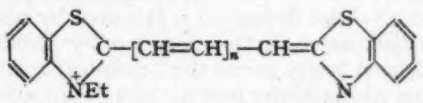
FIG. 4.

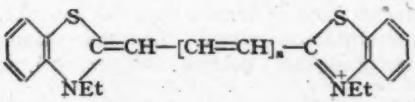
αγ-Dicarbalkoxyglutaconic esters.

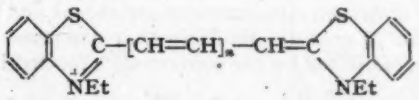


1. *Ethyl ester in* cyclo*hexane.*
2. ,, ,, ,, *alcohol* (5×10^{-4} M.).
3. *Methyl* ,, ,, 5% *alcoholic* H_2SO_4.
4. ,, ,, ,, *alcohol* (4×10^{-4} M.).

(IV.) 

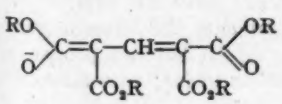
(V.) 

(VI.) 

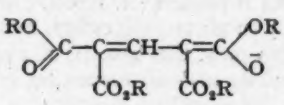
(VII.) 

Brooker has pointed out that for compounds formally conjugated to the same extent, deepening of colour, as regards both λ and ε, is found in those structures which allow of effectively complete resonance degeneracy. The anhydro-base (IV), for example, is not fully mesomeric because the extreme canonical structure (V) is at a higher energy level. The corresponding ethiodide (VI) (a cyanine dye), of equal formal conjugation, is completely valency degenerate because the extreme alternative structure (VII) is now strictly equivalent, and this dye absorbs at considerably longer wave-lengths and also much more intensely than its parent base.

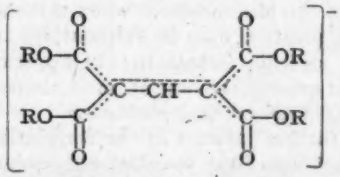
The enol ions of αγ-dicarbalkoxyglutaconic esters are clearly much simpler examples of the cyanine structural system, the two forms (VIII) and (IX) being energetically identical. All the ester groups will participate



(VIII.)



(IX.)

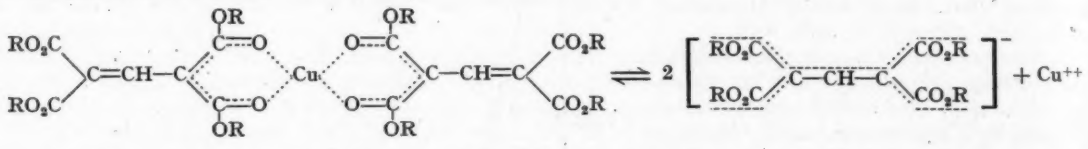


(X.)

in the charge distribution, so the real state of the ion is as schematically shown in (X), in which six electrons are shared over the dotted tracks. This interpretation of the long wave-length absorption also throws light on the general behaviour of glutaconic ester-type tautomerides which, in short, is determined by the high stability of the enol anion.*

* The complete mesomerism of symmetrically substituted glutaconic acid derivatives, which is the basis of the "reversion to type," has been previously recognised in the chemical sense both implicitly and explicitly(Thorpe, Presidential Address, J., 1931, 1002; Evans, Rydon, and Briscoe, J., 1939, 1673). The structural relationship with the

(iii) The reduced absorption of solutions of the copper derivatives must be attributed to complex formation where co-ordination of the metal atom tends to localise the anionic charge in its neighbourhood. Two of the four extreme canonical structures will thus be preferentially stabilised, a process known to result in short-wave spectral displacement (Brooker, *loc. cit.*; Brooker and Sprague, *J. Amer. Chem. Soc.*, **1941**, **63**, 3214). The equilibrium may be written :

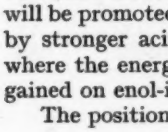


where reduced resonance in the chelated organic residue is compensated for by increased resonance in the metallic valencies.

(iv) In ketones proper, enolisation is promoted by non-ionising solvents and repressed by hydroxylic solvents, *i.e.*, the reverse of the behaviour shown by the tetra-esters (II) which enolise exclusively in the latter media, and the equilibrium is not usually affected by dilution with the same solvent or by addition of acid (Morton and Rosney, J., 1926, 706; Morton, Hassan, and Calloway, *loc. cit.*; cf. however, Hantzsch, *loc. cit.*). Differences between these two tautomeric types, however, are not as fundamental as the solvent effects cursorily suggest.

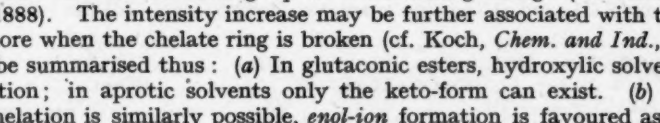
The equilibrium in the glutaconic esters is represented by $AH \rightleftharpoons A^- + H^+$, where AH and A^-, the keto-form and enol ion respectively, are the sole recognisable entities. There are no absorption bands corresponding to a third tautomer such as the undissociated enol. When A^- is sufficiently stabilised by resonance, enolisation will be promoted by proton acceptors to an extent depending on their basic strength, and inhibited completely by stronger acids and by aprotic solvents. The equilibrium is merely that of a simple acid–base system, where the energy of ionisation of the C–H bond is reduced by an amount approaching the resonance energy gained on enol-ion formation.

The position is less straightforward in ketones proper, since the hydrogen enol now has real existence. The



equilibria are as shown in the inset, where KH, E–H, and E^- are the keto-form, enol, and enolate ion, respectively. The enol is energetically stabilised either by intramolecular (Sidgwick, J., 1925, **127**, 907) or, less commonly, by intermolecular (Hunter, *Chem. and Ind.*, 1941, **60**, 32) hydrogen bonding. In consequence, the chelated enols, in common with other hydrogen-bonded structures such as salicylaldehyde and *o*-hydroxyacetophenone, absorb at longer wave-lengths than their *O*-alkylated derivatives (Morton, Hassan, and Calloway, *loc. cit.*; Morton and Stubbs, J., 1940, 1354). Enol formation is favoured by conditions of minimum polarity; hydroxylic solvents, either by acting as alternative electron donors or by effecting charge distribution, inhibit severely. In the glutaconic esters, a hydrogen bridge across the 7-membered resonating unit (see X) is highly improbable stereochemically, while bonding within either malonic end group would interfere with full molecular mesomerism. Hence, the conditions for hydrogen enol stability are absent and in solvents such as hexane only the keto-structure exists.

Equilibrium (*z*) exactly simulates that described for the glutaconic esters. The absorption bands of the enol ions (E^-), exhibited by the sodium salts formed in water or alcohol (Morton *et al.*, *loc. cit.*), occur at longer



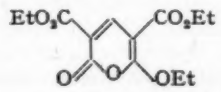
wave-lengths and have much greater intensity than those of the chelated hydrogen enols. This is probably due to fuller mesomerism and to the setting up of a resonating charge (cf. Pauling, Gilman's "Organic Chemistry," 1938, p. 1888). The intensity increase may be further associated with the greater spatial elongation of the chromophore when the chelate ring is broken (cf. Koch, *Chem. and Ind.*, **1942**, **61**, 273).

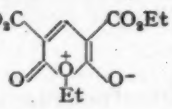
The position may be summarised thus: (*a*) In glutaconic esters, hydroxylic solvents and bases in general favour *enol-ion* formation; in aprotic solvents only the keto-form can exist. (*b*) In ketones proper, and malonic ester where chelation is similarly possible, *enol-ion* formation is favoured as in (*a*); aprotic solvents promote *hydrogen enol* formation.

Of further interest in the correlation of absorption spectra with structure in highly resonating systems is the spectrum of the so-called ethoxy-lactone (XI) obtained by loss of ethyl alcohol when attempts are made to distil ethyl $\alpha\gamma$-dicarbethoxyglutaconate (see experimental section). With bands at 2500 and 3550 A. of practically identical intensity (Fig. 5), the spectrum in *cyclo*hexane is not dissimilar to the reported spectra of other α-pyrones (Haworth, Hirst, and Jones, J., 1938, 710; Haworth, Heslop, Salt, and Smith, J., 1944, 217), although

cyanines and the recognition of charge-resonance spectra in simple aliphatic systems have not been pointed out except in the paper of Schwarzenbach *et al.* (*Helv. Chim. Acta*, 1944, **27**, 576) which appeared after the completion of this work. The deductive approach of the Swiss authors presents a wider theoretical survey, but experimental corroboration is still limited. It is of interest that the sodium enolate of glutacondialdehyde is found to absorb intensely at 3650 A.

the intense near ultra-violet absorption is again notable. Guthzeit and Dressel (*Ber.*, 1889, **22**, 1413) found that the compound was decomposed by alcohol, but we have yet to obtain evidence that it exists at all in

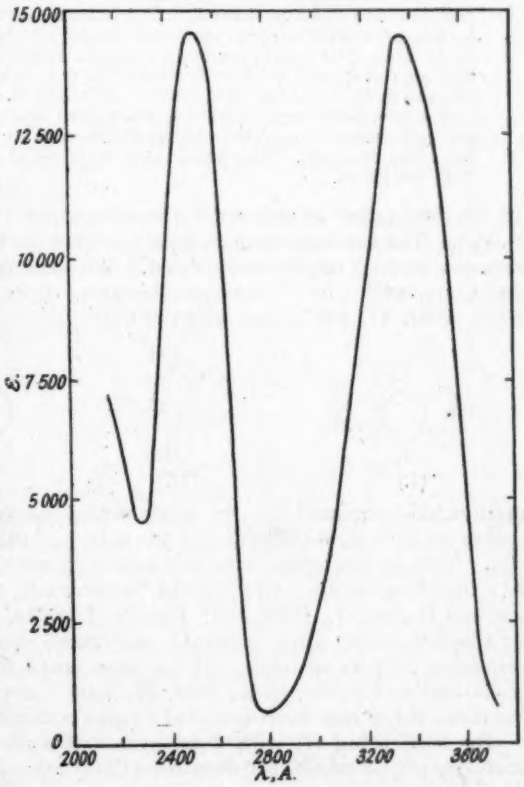
(XI.) 

 (XII.)

hydroxylic solvents. If dissolved in alcohol and immediately examined spectroscopically, only the original glutaconic ester can be detected, and this finds a parallel in the ferric chloride reaction which, entirely absent in *cyclo*hexane, becomes identical with that of the glutaconic ester on the addition of a few drops of alcohol. We suggest tentatively that the compound may really be the internal salt (XII). This symmetrical structure is highly degenerate in the distribution of the negative charge, and it follows that hydroxylic solvents will effect decomposition subsequent to internal ionic dissociation. Further pursuit of this topic awaits more extensive knowledge of the chemistry and spectroscopy of related lactones and their derivatives than it has yet been possible to obtain.

FIG. 5.

Lactone from ethyl dicarbethoxyglutaconate, in cyclo*hexane solution.*



EXPERIMENTAL.

The spectrographic technique was as detailed by Bateman and Koch (*loc. cit.*). Compounds not otherwise described were those employed for *X*-ray examination and are analytically specified in Part IV.

Sodio-tetra-esters (II, X = Na).—(i) The ethyl ester, prepared according to Ingold and Perren (J., 1921, 1582) and recrystallised four times from aqueous alcohol, had m. p. 260°. (ii) Guthzeit, Weiss, and Schaefer (*J. pr. Chem.*, 1909, **80**, 439) were unable to crystallise the crude methyl ester obtained from condensation of methyl sodiomalonate with chloroform, but describe an extraction procedure for isolating the pure sodio-derivative, m. p. 247—248°. We were unable to obtain pure specimens in this way (Found: C, 43·25; H, 4·4; Na, 8·4. Calc. for $C_{11}H_{13}O_8Na$: C, 44·5; H, 4·4; Na, 7·75%), although m. p.'s as high as 258—259° were observed. The pure compound was prepared by shaking the pure parent ester (II, R = Me, X = H; 2 g.) in ether with sodium carbonate (0·38 g.) in water, evaporating the aqueous layer under reduced pressure, extracting the residue with acetone, isolating the extract, and repeating the extraction. This solution yielded a very pale yellow powder, m. p. 264° (Found: C, 44·75; H, 4·4; Na, 7·5%).

Copper salts of the tetra-esters (II, X = ½Cu). (i) That from the ethyl ester, recrystallised three times from ethyl alcohol, had m. p. 177°. (ii) For the preparation of the *salt* from the methyl ester, an aqueous solution of the crude sodio-compound was treated with aqueous cupric sulphate, and the precipitate crystallised three times from ethyl alcohol, m. p. 246—248° [Found: C, 43·1; H, 4·35; Cu, 10·5. $(C_{11}H_{13}O_8)_2Cu$ requires C, 43·2; H, 4·3; Cu, 10·4%].

Dicarbalkoxyglutaconic Esters (II, X = H).—(i) *Ethyl ester.* Evaporation of the extract after decomposing the pure sodio-compound with dilute aqueous acid in the presence of ether gave a clear syrup (Found: C, 54·35; H, 6·75. Calc. for $C_{15}H_{22}O_8$: C, 54·5; H, 6·7%) whose spectrum was virtually identical with that of the pure crystalline methyl ester. As the usual distillation technique under reduced pressure causes decomposition with pyrone formation, short path, non-ebullioscopic, distillation between surfaces at 90° and — 78° at a pressure of 10^{-5} mm. of mercury was carried out. Even this distillate contained 3% of pyrone as estimated by the very sensitive spectroscopic method (Found: C, 54·55; H, 6·7%. Cf. analysis of the pyrone). (ii) *Methyl ester.* The recrystallised copper derivative, dissolved in chloroform, was shaken with dilute aqueous sulphuric acid until the organic layer became colourless. After being dried and evaporated under reduced pressure, the chloroform solution yielded a colourless syrup which eventually crystallised, m. p. 49°. Recrystallisation from ether–ligroin gave the pure ester, m. p. 50—51° (Found: C, 48·25; H, 5·15. Calc. for $C_{11}H_{14}O_8$: C, 48·2; H, 5·15%). Ingold, Parekh, and Shoppee give m. p. 43°. Submitted to non-ebullioscopic distillation (surface temperatures 80° and — 78°), the distillate in this case was free from pyrone and was spectrally identical with the pure crystals.

Pyrone (XI or XII).—The solid obtained on distillation of the ethyl tetra-ester under 11 mm. was recrystallised successively from ether and *cyclo*hexane and had m. p. 95° (Found: C, 54·9; H, 5·75. Calc. for $C_{11}H_{14}O_7$: C, 54·8; H, 5·6%).

Ethyl αγ-Dicarbethoxy-α-ethylglutaconate.—Prepared by Thole and Thorpe's method (J., 1911, **99**, 2187), this had b. p. 214°/25 mm. (Found: C, 57·0; H, 7·4. Calc. for $C_{17}H_{26}O_8$: C, 57·0; H, 7·3%). Selective absorption was entirely absent in *cyclo*hexane as well as in alcoholic solution. A fractionated specimen, b. p. 120—121°/0·05 mm., prepared according to Guthzeit and Dressel (*Ber.*, 1890, **23**, 3179), gave incorrect analyses (Found: C, 57·8, 58·0; H, 7·5, 7·6%) and reduced permanganate in acetone 10—15 times as rapidly as the pure compound but its absorption was only slightly greater. The nature of the impurity was not ascertained.

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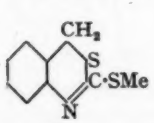
[*Received, November 14th*, 1944.]

59. *Thiazinocyanines. Part IV. Simple Cyanines containing the 2 : 4-Benzthiazine Nucleus.*

By Bernard Beilenson, Frances M. Hamer, and Russell J. Rathbone.

Three 3-alkylthio-2 : 4-benzthiazine alkiodides were prepared. Five bases, of which methincyanines are quaternary salts, were synthesised from 3-alkylthio-2 : 4-benzthiazine and various heterocyclic quaternary salts having a reactive methyl group, followed by alkali. Another was prepared from 3-methyl-2 : 4-benzthiazine and a 2-methylthioquinoline quaternary salt. In these, the alkyldihydro-structure was in the nucleus other than benzthiazine. One of the alternative type was synthesised from 3-alkylthio-2 : 4-benzthiazine methiodide and quinaldine, and one having two benzthiazine nuclei from a 3-methylthio-2 : 4-benzthiazine salt and 3-methyl-2 : 4-benzthiazine. Ten simple cyanines of various types, but all having one 2 : 4-benzthiazine nucleus, were synthesised from 3-alkylthio-2 : 4-benzthiazine alkiodide and various heterocyclic quaternary salts having a reactive methyl group, in the presence of a condensing agent; one of them was also prepared from a dye base by the action of methyl sulphate and potassium iodide. Attempts to prepare methincyanines of this series by interaction of 3-ethylthio-2 : 4-benzthiazine, ethyl *p*-toluenesulphonate, and a heterocyclic base having a reactive methyl group, followed by potassium iodide, led to hydriodides and not ethiodides. These hydriodides were shown to have the alkyldihydro-structure in the nucleus other than benzthiazine. The absorption maxima of the various bases and dyes were compared and sensitising data are given.

In the first paper of this series (Beilenson and Hamer, J., 1942, 98), we mentioned 3-methylthio-2 : 4-benzthiazine (I) as an intermediate likely to give quaternary salts whence cyanine dyes containing the 2 : 4-benzthiazine nucleus might be obtained. We have prepared the necessary 3-thiol-2 : 4-benzthiazine, which Paal and Commerell called " thiocumothiazone," from *o*-aminobenzyl alcohol, by slightly modifying their method (*Ber.*, 1894, **27**, 2427), and whereas they subsequently used methyl iodide and alkali to convert it into the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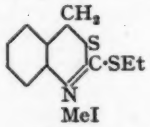
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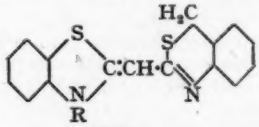
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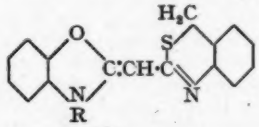
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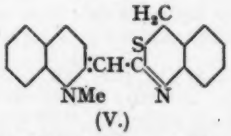
methylthio-compound (I), we used methyl sulphate and alkali. By the action of methyl iodide, (I) was converted into its *methiodide* but the action of ethyl iodide resulted in *3-ethylthio-2 : 4-benzthiazine methiodide* (II). This is analogous with the rearrangement of alkyl groups that occurs when ethyl iodide acts upon 2-methylthioquinoline, 2-methylthiobenzthiazole, and 2-methylthiodihydro-1 : 3-thiazine, respectively (Beilenson and Hamer, J., 1939, 143; Sexton, J., 1939, 470; Hamer and Rathbone, J., 1943, 243). From 3-thiol-2 : 4-benzthiazine, ethyl sulphate and alkali, there was prepared *3-ethylthio-2 : 4-benzthiazine*, which was converted into its *ethiodide*. It has been noted that in preparing 3-methyl-2 : 4-benzthiazine by the method of Gabriel and Posner (*Ber.*, 1894, **27**, 3509) the yields were erratic (Beilenson and Hamer, J., 1942, 98), but the method has now been modified to give consistently good yields.

By condensing (I) with 2-methylbenzthiazole metho-*p*-toluenesulphonate, and by condensing its ethyl analogue with 2-methylbenzthiazole etho-*p*-toluenesulphonate, methanethiol or ethanethiol, respectively, was eliminated, and by subsequent treatment with alkali, two *dye bases* were obtained (III; R = Me) and (III; R = Et). By use of 2-methyl-4 : 5-benzbenzthiazole etho-*p*-toluenesulphonate, the 4 : 5-benz-derivative of the latter was also prepared. The yields varied from 28—40%. However, we were unable to obtain a base isomeric with (III; R = Me), but carrying the *N*-methyl group in the benzthiazine nucleus, by condensing the methiodide of (I) with 2-methylbenzthiazole. By condensing (I) with 2-methylbenzoxazole methiodide and ethiodide, respectively, the *dye bases* (IV; R = Me) and (IV; R = Et) were prepared, the latter being purified through its *hydriodide*, but here again an attempt to obtain the isomer of the former, by condensing the metho-*p*-toluenesulphonate of (I) with 2-methylbenzoxazole, gave a negative result.

We failed to make the base (V) from (I) with quinaldine metho-*p*-toluenesulphonate, but were able to prepare it in 60% yield from 3-methyl-2 : 4-benzthiazine and 2-methylthioquinoline metho-*p*-toluene-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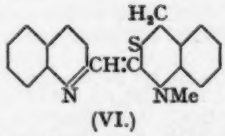
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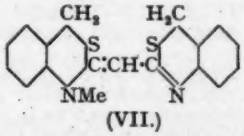

(VII.)

sulphonate, followed by alkali. In this case we were also successful in preparing the isomeric base (VI), although only in 14% yield, from (I) and methyl *p*-toluenesulphonate, followed by quinaldine. From (I)

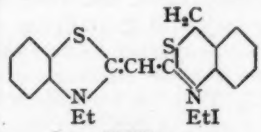
and methyl *p*-toluenesulphonate, followed by 3-methyl-2 : 4-benzthiazine, and by alkali, the base (VII), having two benzthiazine nuclei, was prepared in 30% yield; it was also prepared by condensing the methiodide of (I) with 3-methyl-2 : 4-benzthiazine, followed by alkali, this yield being 17%.

Absorption curves of methyl-alcoholic solutions of the bases were plotted, and the maxima determined. On passing from the oxa- to the thia-series, *i.e.*, from (IV; R = Me) to (III; R = Me) and from (IV; R = Et) to (III; R = Et), the maximum shifted 185 and 220 A. towards the red. Introduction of the 4 : 5-benz-group into (III; R = Et) caused a shift towards the red of 150 A. Acidification of the three thia-bases, namely (III; R = Me), (III; R = Et), and the 4 : 5-benz-derivative of the latter, caused shifts towards the red of 175, 210, and 160 A., respectively. Acidification of the two oxa-bases, namely, (IV; R = Me) and (IV; R = Et), caused shifts towards the red of 130 and 110 A., respectively. On passing from the thia-base (III; R = Me) to the 2′-cyanine base (V), the absorption maximum shifted 475 A. towards the red.

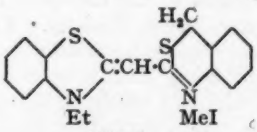
On passing from the 2′-cyanine base (VI) to its isomer (V), the shift towards the red was 600 A. Our colleague Dr. L. G. S. Brooker points out that such a difference in absorption indicates that the benzthiazine nucleus is less basic than the quinoline nucleus, the relationship between the two rings being similar to that between indole and benzthiazole or indole and quinoline, linked in the 4-position (Brooker, Sprague, Smyth, and Lewis, *J. Amer. Chem. Soc.*, 1940, **62**, 1116). Where the maximum of (V) shifted only 200 A. towards the red on acidification, the maximum of (VI) shifted 600 A. On acidifying the base (VII), which has two benzthiazine nuclei, the band became narrower and shifted 365 A. towards the red.

Three of these bases, namely (III; R = Et), its 4 : 5-benz-derivative, and (IV; R = Et), may be compared with three bases of the carbocyanine series, which have already been described (Beilenson and Hamer, J., 1942, 98) and which differ from them only in having two extra methin groups in the chain joining the nuclei. On passing from the present three cyanine bases to their higher vinylene homologues, the absorption maxima shifted 560, 560, and 470 A. towards the red.

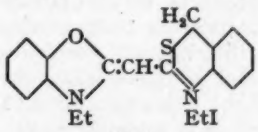
By condensing 2-methylbenzthiazole ethiodide with 3-ethylthio-2 : 4-benzthiazine ethiodide, in the presence of triethylamine in alcohol, the simple cyanine (VIII) was prepared, ethanethiol and hydrogen iodide being eliminated. Use of 2-methyl-6 : 7-benzbenzthiazole ethiodide resulted in its 6 : 7-benz-derivative.



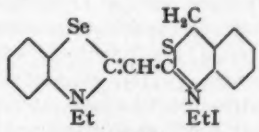
(VIII.)



(IX.)

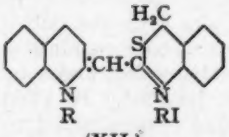


(X.)

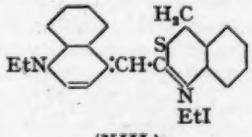


(XI.)

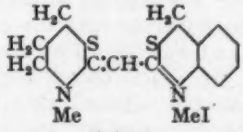
From 2-methylbenzthiazole ethiodide and the methiodide of (I), the simple cyanine (IX) was synthesised. (IX) also resulted on condensing 2-methylbenzthiazole ethiodide with the product obtained by interaction of (I) with ethyl iodide: our conclusion that this interaction involves rearrangement of alkyl groups, leading to (II), was based on this observation and on two other similar ones. By condensing 2-methylbenzoxazole ethiodide and 2-methylbenzselenazole ethiodide, respectively, with 3-ethylthio-2 : 4-benzthiazine ethiodide, (X) and (XI) were prepared, and the 6 : 7-benz-derivative of (X) was also similarly obtained. From quinaldine methiodide and the methiodide of (I), the 2′-cyanine (XII; R = Me) was prepared. From quinaldine ethiodide and lepidine ethiodide, respectively, with 3-ethylthio-2 : 4-benzthiazine ethiodide, the 2′-cyanine (XII; R = Et) and the 4′-cyanine (XIII) were prepared. From 2-methyldihydro-1 : 3-thiazine methiodide



(XII.)



(XIII.)



(XIV.)

(Hamer and Rathbone, J., 1943, 243) and the methiodide of (I), the cyanine (XIV) was obtained in 11% yield. For both oxa-dyes, the yields were 27%, for the 2′-cyanines they were 33% and 52%, 45% for the 4′-cyanine, 61% for the selena-compound, and 42—69% in the four preparations of thia-dyes.

An unsuccessful attempt was made to prepare the cyanine (VIII) from the base (III; R = Et) by heating the latter in a sealed tube with ethyl iodide. Similar negative results were also obtained when attempts were made to arrive at the ethiodide by use of ethyl *p*-toluenesulphonate or ethyl sulphate. However, although we failed to convert the base (III; R = Et) into its ethiodide, we did succeed in converting it into its methiodide (IX) by use of methyl sulphate, followed by potassium iodide. By means of methyl sulphate and potassium iodide we were also able to convert each of the pair of isomers (V) and (VI) into the 2′-cyanine (XII; R = Me). The yield of 2′-cyanine was 36% from (V) but only 20% from (VI) and in the latter case it was accompanied by a less soluble by-product.

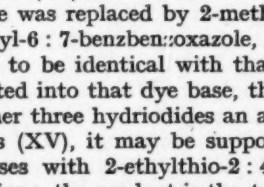
Absorption curves of methyl-alcoholic solutions of the methincyanines were plotted. On passing from the oxa-compound (X) to the thia-compound (VIII), the maximum shifted 400 A. towards the red, but on passing from thia-compound (VIII) to selena-compound (XI) the shift was only 140 A. in the same direction. Introduction of the 6 : 7-benz-group into (X) and (VIII) caused shifts of 210 and 200 A. towards the red.

An acid solution of the base (III; R = Et) had its absorption maximum 35 A. further towards the red than had the cyanine dye (VIII), which is the ethiodide of that base. On passing from the thia-dye (VIII) to the 2'-cyanine (XII; R = Et) and from that to the 4'-cyanine (XIII), the bathochromic shifts were 425 and 330 A. The absorption maximum of the 2'-cyanine (XII; R = Et) lay 75 A. on the short wave-length side of the maximum of an acidified solution of base (V), and 125 A. on the long wave-length side of the maximum of an acidified solution of base (VI).

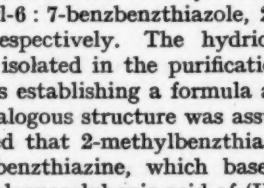
On passing from the methincyanines (X) and (VIII) to the corresponding trimethincyanines, which have previously been described (Beilenson and Hamer, J., 1942, 98), introduction of the extra vinylene group caused a shift towards the red of 1200 A. in each instance.

Analogues of the present methincyanines have already been described, in which the part played by the 2 : 4-benzthiazine nucleus is taken by the dihydro-1 : 3-thiazine nucleus (Hamer and Rathbone, J., 1943, 243). The effect upon the absorption maximum of replacing that simple nucleus by the more complex one may now be found for eight pairs of dyes. The shift is in every instance a bathochromic one. In the oxa-series, on passing from the corresponding simple dyes to (X) and to the 6 : 7-benz-derivative of (X), the shifts are 140 and 240 A., respectively; in the thia-series, on passing from the corresponding simple dyes to (VIII) and to the 6 : 7-benz-derivative of (VIII), the shifts are 260 and 250 A., respectively; in the selena-series, on passing from the simple dye to (XI), the shift is 340 A.; in the 2'-cyanine series the shifts on passing to (XII; R = Me) and to (XII; R = Et) are 125 and 175 A., respectively; in the 4'-cyanine series the shift on passing from the simple dye to (XIII) is 205 A.

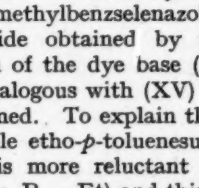
The preparation of simple cyanines by fusing together a heterocyclic base having a reactive alkylthio-group, a heterocyclic base having a reactive methyl group, and alkyl *p*-toluenesulphonate, followed by treatment with a solvent and an acid-binding agent, is one that has been patented (Kendall, B.P. 424,559/1933). In the present series, its attempted application led to curious results. It was noticed in the first place that a better product was obtained when no condensing agent was added after the fusion. The procedure adopted was therefore to fuse together equimolecular amounts of the two bases and 2 mols. of ethyl *p*-toluenesulphonate, dissolve the melt in spirit, and treat it with potassium iodide. Five such preparations yielded crystalline products, which did indeed look like the expected methincyanines, but analysis after recrystallisation showed them to be hydriodides and not ethiodides. Thus fusion of 2-methylbenzthiazole, 3-ethylthio-2 : 4-benzthiazine, and ethyl *p*-toluenesulphonate would have been expected to give the cyanine (VIII), ethanethiol and *p*-toluenesulphonic acid being eliminated: in fact, however, it gave a hydriodide, to which, at first sight, the constitution (XV) might be assigned, though (XVI) is also a possibility. That the constitution really is (XV) and not (XVI) was established, first by conversion of the hydriodide into the base (III; R = Et) by heating with alkali and benzene, and secondly by its preparation from (III; R = Et) by the action of hydriodic acid; in contrast to the breakdown of the hydriodide by alkali, the alkiodide (IX) was resistant to this treatment. Hydriodides were similarly obtained when 2-methylbenzthiazole was replaced by 2-methyl-6 : 7-benzbenzthiazole, 2-methylbenzselenazole, 2-methylbenzoxazole, and 2-methyl-6 : 7-benzbenzoxazole, respectively. The hydriodide obtained by use of 2-methylbenzoxazole proved to be identical with that isolated in the purification of the dye base (IV; R = Et) and was itself converted into that dye base, thus establishing a formula analogous with (XV) as opposed to (XVI). With the other three hydriodides an analogous structure was assumed. To explain the formation of a hydriodide, such as (XV), it may be supposed that 2-methylbenzthiazole etho-*p*-toluenesulphonate is first formed and condenses with 2-ethylthio-2 : 4-benzthiazine, which base is more reluctant to undergo quaternary salt formation; the product is the *p*-toluenesulphonic acid of (III; R = Et) and this, by the action of potassium iodide, is converted into the corresponding hydriodide. Although the hydriodides were the only products isolated and were certainly the main products, it is possible that small amounts of true cyanines were also formed. An exact comparison of the hydriodides and ethiodides as regards melting point, and solubility in methyl alcohol, showed that generalisations as to these properties were not justified. In plotting the absorption curves of the hydriodides it was noticed that sometimes the maximum approximated to that of the ethiodide but sometimes to that of the base. For this reason they were plotted both in basified and in acidified methyl alcohol. The change from alkalinity to acidity always caused a bathochromic shift. This was 130 A. with the oxa-compound, 120 A. with its 6 : 7-benz-derivative, 200 A. with the thia-compound, 250 A. with its 6 : 7-benz-derivative, and 300 A. with the selena-compound. Surprisingly, the absorption maximum of the basified solutions was, in four cases out of five, nearer to that of the ethiodide than was that of the acidified solution.



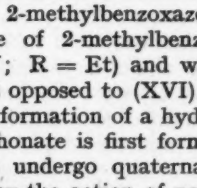
(XV.)



(XVI.)



(XVII.)



(XVIII.)

A pair of dyes, containing the 2 : 4-benzthiazine nucleus, but other than cyanines, was prepared by use of compounds containing a reactive cyclic methylene group (cf. Kendall, B.P. 426,718/1933; Kodak Ltd.,

B.P. 450,958/1934). Thus by condensing the methiodide of (I) with 3-ethylrhodanine and with 4-keto-2-thio-3-ethyltetrahydro-oxazole, respectively, dyes (XVII) and (XVIII) were obtained, in 50% and 49% yields. These same compounds were also prepared by using the salt which results by the action of ethyl iodide on 3-methylthio-2 : 4-benzthiazine, thus providing further evidence that this salt has the structure (II).

When the oxygen atom in the oxazole ring of (XVIII) is replaced by sulphur, giving (XVII), the absorption maximum shifts 330 A. towards the red. We have already described an analogue of (XVII) which contains the dihydro-1 : 3-thiazine nucleus instead of the 2 : 4-benzthiazine nucleus (Hamer and Rathbone, J., 1943, 243). On passing from this earlier dye to the present more complex one, the absorption maximum shifted 80 A. towards the red.

The behaviour of the various dyes towards a gelatino chloride photographic emulsion was examined and it was found that the group comprises some powerful sensitisers. Of the five hydriodides of the methin dye bases, four sensitised much more powerfully than did those methincyanines which were the corresponding ethiodides; with the fifth the action of the hydriodide was a little stronger than that of the ethiodide. It has already been recorded that in the 2 : 4-benzthiazine series the sensitising action of the carbocyanine ethiodides closely approximated to that of the corresponding bases (Beilenson and Hamer, J., 1942, 98). With carbocyanines of the *peri*naphtha-1 : 3-thiazine series it was noted that a methiodide and ethiodide had the same sensitising maximum as the corresponding hydrochloride and base, whilst another pair, consisting of carbocyanine base and hydrochloride, also showed identity of sensitising maxima (Hamer and Rathbone, J., 1943, 487). Our colleague, Dr. B. H. Carroll, has now straightened out what seemed anomalous. By examining the sensitising action of pairs of dye bases and hydrochlorides of other series, he found that the sensitisation appears to be dependent on pH only, regardless of whether the base or its salt is taken. In the present work the sensitising effect of each of the dye bases (III; R = Et) and (IV; R = Et) was found to be similar to that of the respective hydriodide and in the same region as that of the ethiodide, (VIII) and (X), respectively; also the base (III; R = Me) sensitised in the same region as its ethiodide (IX). The sensitising action of (XII; R = Me) resembled that of base (V) but not that of base (VI).

Experimental.

3-Thiol-2 : 4-benzthiazine.—*o*-Aminobenzyl alcohol, alcoholic potassium hydroxide, and carbon disulphide were heated together on the water-bath as described by Paal and Commerell (*Ber.*, 1894, **27**, 2427), but for 18 hours instead of 10. Excess of carbon disulphide was removed by distillation, instead of by steam-distillation, and the filtration before distillation was omitted. Afterwards the potassium salt which separated was filtered off. It was purified by their method of dissolving in dilute potassium hydroxide solution, filtering, and precipitating with acid. The thiol compound was almost white and was obtained in 79% yield, m. p. 160—162°. After recrystallisation from dilute spirit, the m. p. was 166°, as recorded by Paal and Commerell, who obtained 70—80% yields. It should be used at once, as it decomposes on keeping.

3-Methylthio-2 : 4-benzthiazine (I).—3-Thiol-2 : 4-benzthiazine (35 g.; 1 mol.) was dissolved in 10% sodium hydroxide solution (70 c.c.) and methyl sulphate (38 c.c.; 2 mols.) was gradually added with shaking; more sodium hydroxide solution (40 c.c.) was added to keep the mixture alkaline. The resultant solid was filtered off, heated on the water-bath under a vacuum to remove water, and finally vacuum-distilled, being obtained in 82% yield (31 g.). It was analysed by the method of Carius, which method was used throughout this work, except where otherwise stated (Found: S, 32·75. Calc. for $C_9H_9NS_2$: S, 32·85%). B. p. 192°/20 mm., m. p. 70—73°. Paal and Commerell, who prepared it by use of methyl iodide in the presence of alkali, recrystallised it from light petroleum and record an almost theoretical yield, m. p. 73° (*loc. cit.*).

3-Ethylthio-2 : 4-benzthiazine.—3-Thiol-2 : 4-benzthiazine (36·2 g.; 1 mol.) was dissolved in 10% sodium hydroxide solution (80 c.c.) and shaken with ethyl sulphate (26 c.c.; 1 mol.). After standing for an hour, with occasional shaking, the mixture was heated on the water-bath for 30 minutes. Excess of ammonia was added, and the oil extracted with ether. The residue from the dried ethereal extract, after removal of solvent, was vacuum-distilled and thus obtained in 76% yield (31·7 g.) (Found: S, 30·65. $C_{10}H_{11}NS_2$ requires S, 30·65%). The oil had b. p. 193°/14 mm.

3-Methylthio-2 : 4-benzthiazine Methiodide.—3-Methylthio-2 : 4-benzthiazine (5·86 g.; 1 mol.) and methyl iodide (4·5 c.c.; 2·4 mols.) were heated together under reflux for 4 days. The solid was ground with ether and 43% of unchanged base (2·5 g.) was recovered from the ethereal extract. The undissolved residue (5·5 g.) was recrystallised from methyl alcohol (5 c.c. per g.) and gave a 36% yield. Before analysis it was dried to constant weight in a vacuum at 60—80°, which method of drying solids was used throughout this work except where stated otherwise (Found: I, 37·65. $C_{10}H_{12}NIS_2$ requires I, 37·65%). The pale yellow substance had m. p. 163°.

3-Ethylthio-2 : 4-benzthiazine Methiodide (II).—After 3-methylthio-2 : 4-benzthiazine (9·9 g.; 1 mol.) and ethyl iodide (4·8 c.c.; 1·2 mols.) had been heated in a sealed tube at 100° for 16 hours, the dirty product was much improved by washing with acetone (13·1 g. obtained). By rapid recrystallisation from methyl alcohol (30 c.c.), it was obtained in 53% yield (9·6 g.) (Found: I, 36·35. $C_{11}H_{14}NIS_2$ requires I, 36·15%). The pale yellow prisms had m. p. 138° (decomp.).

3-Ethylthio-2 : 4-benzthiazine Ethiodide.—3-Ethylthio-2 : 4-benzthiazine (20·9 g.; 1 mol.), ethyl iodide (9·6 c.c.; 1·2 mols.), and a little quinol (0·05 g.) were heated together in a sealed tube at 100° for 2 days. The product was treated with absolute ether, and the resultant solid recrystallised from absolute alcohol (80 c.c.) with charcoal (1 g.). The yield of yellow crystalline product was 30% (22·5 g.) (Found: I, 34·9. $C_{12}H_{16}NIS_2$ requires I, 34·75%). M. p. 129° (decomp.).

3-Methyl-2 : 4-benzthiazine.—*o*-Aminobenzyl chloride hydrochloride (4 g.; 1 mol.), thioacetamide (2 g.; 1·2 mols.), anhydrous potassium carbonate (180-mesh; 13·6 g.; 4·4 mols.), and absolute ethyl alcohol (40 c.c.) were boiled together under reflux for 45 minutes. The alcohol was distilled off, and the residue steam-distilled. The resultant oil solidified on cooling and was filtered off and finally dried in a vacuum desiccator, being obtained in 64% yield (2·34 g.). It was almost colourless, m. p. 42—43°, whereas Gabriel and Posner give m. p. 45—46° for the base, which they prepared by heating the reactants without solvent or condensing agent (*Ber.*, 1894, **27**, 3509). By distillation in a vacuum, the yield was reduced to 47% but the m. p. was unchanged, b. p. 155—160°/15 mm. (Found for material dried in a vacuum to constant weight: S, 19·7. Calc. for C_9H_9NS: S, 19·65%).

Methin-[2-(*3-methyldihydrobenzthiazole*)][3-(2 : 4-*benzthiazine*)] (III; R = Me).—2-Methylbenzthiazole metho-*p*-toluenesulphonate (3·35 g.; 1 mol.) and 3-methylthio-2 : 4-benzthiazine (1·95 g.; 1 mol.) were fused together at 160° for 30 minutes. The product was heated with 10% sodium hydroxide solution and the resultant *base* when cold was filtered off and washed with water and with acetone (2·62 g. obtained). After two recrystallisations from acetone (20 c.c. per g.), the yield was

36% (1·12 g.) (Found : S, 20·55. $C_{17}H_{14}N_2S_3$ requires S, 20·7%). The lemon-yellow crystals had m. p. 154°. The absorption maximum of a methyl-alcoholic solution was at 4025 A. and shifted to 4200 A. on addition of sulphuric acid (5 g. per 100 c.c.). It is a good sensitiser for a gelatino silver chloride emulsion, giving a maximum at 4600, the sensitivity extending past 5100 A.

Methin-[(2-(3-*ethyldihydrobenzthiazole*)][3-(2 : 4-*benzthiazine*)] (III; R = Et).—The base, similarly prepared from 2-methylbenzthiazole etho-*p*-toluenesulphonate and 3-ethylthio-2 : 4-benzthiazine, followed by sodium hydroxide solution, was purified by washing with water and grinding with acetone. It was recrystallised from acetone (20 c.c. per g.) and thus obtained in 40% yield (Found : S, 20·0. $C_{18}H_{16}N_2S_2$ requires S, 19·75%). The lemon-yellow crystals had m. p. 143°. The absorption maximum was at 4090 A. and shifted to 4300 A. on addition of sulphuric acid (5 g. per 100 c.c.). It is a strong sensitiser for a chloride emulsion, having its maximum effect at 4700 A.

Methin-[2-(3-*ethyldihydro*-4 : 5-*benzbenzthiazole*)][3-(2 : 4-*benzthiazine*)].—In condensing 2-methyl-4 : 5-benzbenzthiazole etho-*p*-toluenesulphonate (3·99 g.) and 3-methylthio-2 : 4-benzthiazine, heating was at 145—150° for 2½ hours. The reaction mixture was subsequently heated with sodium hydroxide solution and extracted with benzene. The product obtained on removal of benzene from the dried extract was recrystallised from ethyl acetate (120 c.c.). After washing with cold spirit, the yield was 28% (Found : S, 17·3. $C_{22}H_{18}N_2S_2$ requires S, 17·15%). The brown crystals with a steely reflex had m. p. 206—207°. A methyl-alcoholic solution had its absorption maximum at 4240 A.; on addition of sulphuric acid (5 g. per 100 c.c.) the maximum shifted to 4400 A. The base sensitised a chloride emulsion strongly with a maximum at 4700 A., its action extending to 5200 for moderate exposures.

Methin-[2-(3-*methyldihydrobenzoxazole*)][3-(2 : 4-*benzthiazine*)] (IV; R = Me).—3-Methylthio-2 : 4-benzthiazine (1·95 g.) and 2-methylbenzoxazole methiodide were heated together at 155—160° for 2 hours, and the product was boiled and stirred with benzene (30 c.c.) and 40% sodium hydroxide solution (15 c.c.) for 15 minutes. The product (0·94 g.) obtained from the dried benzene extract was recrystallised from acetone (10 c.c.) and thus obtained in 17% yield (0·50 g.) (Found : S, 11·15. $C_{17}H_{14}ON_2S$ requires S, 10·9%). M. p. 150°. The absorption maximum of a methyl-alcoholic solution was at 3840 A. and on acidification shifted to 3970. The base was a powerful sensitiser towards a chloride emulsion. The maximum was at 4300 A. and its action extended to 4700.

Methin-[2-(3-*ethyldihydrobenzoxazole*][3-(2 : 4-*benzthiazine*)] (IV; R = Et).—After 3-methylthio-2 : 4-benzthiazine (3·90 g.; 1 mol.) had been similarly heated with 2-methylbenzoxazole ethiodide, and the product heated with benzene and alkali, the syrupy residue from the benzene extract was taken up in hot spirit, acidified with hydrochloric acid (1·2 mols.), and treated hot with aqueous potassium iodide (2 mols.). The precipitated *hydriodide* was washed with water and ground with acetone (12 c.c.), being obtained in 31% yield. After recrystallisation from methyl alcohol (85 c.c. per g.), the yield was 24% (Found : I, 28·95. $C_{18}H_{17}ON_2IS$ requires I, 29·1%). M. p. 278° (decomp.) with previous shrinking. The hydriodide (2·58 g.) was boiled and stirred with benzene and alkali. The residue from the dried benzene extract, after removal of solvent, was taken up in ethyl acetate (5 c.c.), precipitated with light petroleum (b. p. 40—60°) (25 c.c.), and finally recrystallised from spirit (2½ c.c.); the amount of *base* (0·78 g.) corresponded with a 43% conversion (Found : S, 10·3. $C_{18}H_{16}ON_2S$ requires S, 10·4%). The yellow product had no definite m. p. but softened at 74°, melted from 85—88° but not to a clear drop, and frothed up at about 110°. A methyl-alcoholic solution had its absorption maximum at 3870 A. On addition of sulphuric acid (5 g. per 100 c.c.) it shifted to 3980. The base was a good sensitiser towards a chloride emulsion. The maximum was at 4300 A. and its action extended to 4650. The spirit filtrate from the base was treated hot with concentrated hydrochloric acid (1 c.c.); the *hydrochloride* crystallised on cooling, the amount (0·40 g.) corresponding with a 20% conversion. It was recrystallised from methyl alcohol (2 c.c.) (0·20 g. obtained) (Found : Cl, 10·25. $C_{18}H_{17}ON_2ClS$ requires Cl, 10·3%). The yellow crystals melted at about 229° (decomp.) with previous softening.

Methin-[2-(1-*methyldihydroquinoline*)][3-(2 : 4-*benzthiazine*)] (V).—2-Methylthioquinoline (1·75 g.; 1 mol.) and methyl *p*-toluenesulphonate (1·86 g.; 1 mol.) were heated together at 145° for 1½ hours, 3-methyl-2 : 4-benzthiazine (1·63 g.; 1 mol.) then added, and heating continued for 10 minutes. The product was stirred with hot spirit (20 c.c.) and poured into aqueous ammonia (30 c.c.; *d* 0·880). The crude base was filtered off when cold and washed with water and spirit (2·55 g. obtained). It was recrystallised from spirit (20 c.c. per g.) and thus obtained in 60% yield (Found : S, 10·65. $C_{19}H_{16}N_2S$ requires S, 10·55%). The bright red crystals had m. p. 132°. The broad absorption band had its maximum at 4500 A. On addition of sulphuric acid (5 g. per 100 c.c.), the colour did not deepen, but the maximum shifted to 4700 A., with an inflexion at 4500, and the band became narrower. In a gelatino silver chloride emulsion the base sensitised with maxima at 4500 and 5000 A., the action extending to 5700. In a gelatino silver bromide emulsion the sensitising action extended to 5500 A.

Methin-[2-*quinoline*][3-(4-*methyldihydro*-2 : 4-*benzthiazine*)] (VI).—3-Methylthio-2 : 4-benzthiazine (1·95 g.) and methyl *p*-toluenesulphonate were heated together at 145—150°, then quinaldine was added and the mixture heated. The product was dissolved in hot spirit and poured into aqueous ammonia. When cold, the resultant oil was treated with cold spirit, which converted it into solid (0·86 g.). After recrystallisation from methyl alcohol (45 c.c.), the yield was 14% (0·44 g.) (Found : S, 10·6. $C_{19}H_{16}N_2S$ requires S, 10·55%). The yellow crystals had m. p. 139° (decomp.). The absorption maximum of the methyl-alcoholic solution was at 3900 A. On addition of sulphuric acid (5 g. per 100 c.c.) there was deepening in colour and the maximum shifted to 4500 with a secondary band at 4350 A. In a gelatino silver chloride emulsion the base was a good sensitiser with maxima at 4350 and 4700 A. Sensitisation was fairly even up to 4850, trailing off to 5150 A.

Methin-[3-(2 : 4-*benzthiazine*)][3-(4-*methyldihydro*-2 : 4-*benzthiazine*)] (VII).—3-Methylthio-2 : 4-benzthiazine (1·95 g.) and methyl *p*-toluenesulphonate were heated together at 150—160° for 3 hours, 3-methyl-2 : 4-benzthiazine added, and heating continued for one hour. The product was heated with sodium hydroxide solution, and the base extracted with benzene. After removal of solvent from the dried extract, the residual oil was dissolved in acetone (7 c.c.), and the solution treated with water (7 c.c.). The aqueous layer was decanted from the paste, which solidified on stirring with cold ethyl acetate (1·71 g. obtained). By crystallisation from ethyl acetate (27 c.c.), it was obtained in 30% yield (0·97 g.). (Found : S, 19·75. $C_{18}H_{16}N_2S_2$ requires S, 19·65%). The yellow crystals had m. p. 162° (decomp.). The absorption maximum of a methyl-alcoholic solution was at 3780 A. On addition of sulphuric acid (10 g. per 100 c.c.), the yellow solution deepened in colour, the band became narrower, and the maximum shifted to 4145 A. The base sensitised a chloride emulsion strongly, the maximum lying at 4400 A. and sensitisation extending past 4900. It was also prepared from 3-methylthio-2 : 4-benzthiazine methiodide and 3-methyl-2 : 4-benzthiazine, followed by sodium hydroxide and chloroform; after recrystallisation from ethyl acetate it was obtained in 17% yield.

[2-(3-*Ethylbenzthiazole*)][3-(4-*ethyl*-2 : 4-*benzthiazine*)]*methincyanine Iodide* (VIII).—2-Methylbenzthiazole ethiodide (1·53 g.; 1 mol.), 3-ethylthio-2 : 4-benzthiazine ethiodide (1·83 g.; 1 mol.), and triethylamine (0·75 c.c.; 1·1 mols.) in absolute alcohol (20 c.c.) were boiled and stirred together for 2 minutes. The washed dye (2·12 g.) was recrystallised from methyl alcohol (40 c.c. per g.) and obtained in 65% yield (1·57 g.) (Found : I, 26·45. $C_{20}H_{21}N_2IS_2$ requires I, 26·45%). The orange-yellow crystals had m. p. 239° (decomp.). The absorption maximum of a methyl-alcoholic solution was at 4200 A. It was a moderate sensitiser with maximum at 4600.

[2-(3-*Ethyl*-6 : 7-*benzbenzthiazole*)][3-(4-*ethyl*-2 : 4-*benzthiazine*)]*methincyanine Iodide*.—When 2-methyl-6 : 7-benzbenzthiazole ethiodide was used instead of 2-methylbenzthiazole ethiodide and the washed product recrystallised from methyl

alcohol (410 c.c. per g.), the yield was 63% (Found: I, 24·05. $C_{24}H_{23}N_3IS_2$ requires I, 23·95%). The orange-yellow crystals had m. p. 270° (decomp.). The absorption maximum of a methyl-alcoholic solution was at 4400 A. It was a moderate sensitiser with its maximum at 4800 A., the sensitising action extending to 5200.

[2-(3-*Ethylbenzthiazole*)][3-(4-*methyl*-2 : 4-*benzthiazine*)]*methincyanine Iodide* (IX).—The dye obtained by condensing 2-methylbenzthiazole ethiodide and 3-methylthio-2 : 4-benzthiazine methiodide in alcohol, in the presence of triethylamine, was recrystallised from methyl alcohol (130 c.c. per g.) and thus obtained in 69% yield (Found: I, 27·35. $C_{19}H_{19}N_3IS_3$ requires I, 27·2%). The bright yellow crystalline product had m. p. 238° (decomp.). The absorption maximum of a methyl-alcoholic solution was at 4200 A. It was a fairly good sensitiser with its maximum in a chloride emulsion at 4600 A.

The same dye was obtained by reaction of 2-methylbenzthiazole ethiodide and potassium carbonate in alcohol with the quaternary salt prepared from 3-methylthio-2 : 4-benzthiazine and ethyl iodide, being obtained in 42% yield after two recrystallisations (Found: I, 27·3%). M. p. and mixed m. p. with other specimen, 239° (decomp.). It was also prepared by heating methin-[2-(3-ethylbenzthiazole)][3-(2 : 4-benzthiazine)] (1·62 g.; 1 mol.) at 100° for an hour with methyl sulphate (0·62 g.; 1 mol.), which had been neutralised and dried by means of sodium bicarbonate and anhydrous sodium sulphate. The product was dissolved in hot spirit and treated with a hot solution of potassium iodide (4 g.) in water (10 c.c.). The orange solid was filtered off, washed with water (1·76 g. obtained), and recrystallised from methyl alcohol, being obtained in 58% yield (1·36 g.) (Found: I, 27·35%). The m. p., 222° (decomp.), was below that of the other sample, but the mixed m. p. was 222—224°. The absorption curves were identical.

To compare with the behaviour of the hydriodide, the present ethiodide (1 g.) prepared by the first method was boiled and stirred with benzene (20 c.c.) and 10% sodium hydroxide solution (20 c.c.) for an hour, but solution was incomplete and 30% of the dye was recovered unchanged. The benzene layer was washed and dried and the solvent was removed but only a sticky solid, m. p. about 98°, was obtained from it (0·5 g.).

[2-(3-*Ethylbenzoxazole*)][3-(4-*ethyl*-2 : 4-*benzthiazine*)]*methincyanine Iodide* (X).—After 2-methylbenzoxazole ethiodide (2·89 g.), 3-ethylthio-2 : 4-benzthiazine ethiodide, and triethylamine had been boiled together in absolute alcohol (10 c.c.) for 7 minutes, the liquid was cooled and treated with excess of ether. The resultant oil solidified on treatment with water. The solid was recrystallised from methyl alcohol (15 c.c.) and thus obtained in 27% yield (1·25 g.) (Found: I, 27·4. $C_{20}H_{21}ON_2IS$ requires I, 27·35%). The yellow crystals had m. p. 277° (decomp.). The absorption maximum of a methyl-alcoholic solution was at 3800 A. It was a moderate sensitiser with its maximum at 4250 A., its action extending to 4500.

[2-(3-*Ethyl*-6 : 7-*benzbenzoxazole*)][3-(4-*ethyl*-2 : 4-*benzthiazine*)]*methincyanine Iodide*.—Prepared from 2-methyl-6 : 7-benzbenzoxazole ethiodide (3·39 g.), 3-ethylthio-2 : 4-benzthiazine ethiodide, and triethylamine in alcohol, with heating for 3 minutes, the washed solid (1·9 g.) was recrystallised from methyl alcohol (80 c.c. per g.) and thus obtained in 27% yield (1·37 g.) (Found: I, 24·6. $C_{24}H_{23}ON_2IS$ requires I, 24·7%). The yellow crystals had m. p. 257° (decomp.). The absorption maximum of their methyl-alcoholic solution was at 4010 A. It was a powerful sensitiser with its maximum at 4500 A. The sensitisation extended to 4800.

[2-(3-*Ethylbenzselenazole*)][3-(4-*ethyl*-2 : 4-*benzthiazine*)]*methincyanine Iodide* (XI).—On boiling 2-methylbenzselenazole ethiodide (3·52 g.) with 3-ethylthio-2 : 4-benzthiazine ethiodide, in the presence of triethylamine in alcohol, dye was at once precipitated, and boiling was continued for 1 minute only. The washed product (4·46 g.) was recrystallised from methyl alcohol (90 c.c. per g.) and thus obtained in 61% yield (3·21 g.) as yellow crystals (Found: I, 24·15. $C_{20}H_{21}N_2ISSe$ requires I, 24·05%). M. p. 234° (decomp.). The absorption maximum of a methyl-alcoholic solution was at 4340 A. The dye was a weak sensitiser with its maximum at 4750 A., the sensitisation extending to 5100.

[2-(1-*Methylquinoline*)][3-(4-*methyl*-2 : 4-*benzthiazine*)] *methincyanine Iodide* (XII; R = Me).—Methin-[2-(1-methylquinoline)][3-(2 : 4-benzthiazine)] (V) (1·52 g.; 1 mol.) was heated with dry, neutral methyl sulphate (0·5 c.c.; 1 mol.) on a steam-bath for an hour. The orange melt solidified on cooling. It was dissolved in hot spirit and treated with a hot solution of potassium iodide (3·3 g.; 4 mols.) in water (5 c.c.). The resultant solid was filtered off (2·1 g. obtained) and twice recrystallised from methyl alcohol (10 c.c. per g.), giving a 36% yield (0·8 g.) (Found for material dried in a vacuum at 60°: I, 28·55. $C_{20}H_{19}N_2IS$ requires I, 28·45%). The reddish-orange crystals had m. p. 107°, but subsequently solidification took place, followed by melting at 227° (decomp.). The absorption maximum of a methyl-alcoholic solution was at 4575 A. The dye was a weak sensitiser with maxima at 4450 and 4900 A., the action falling off gradually to 5400. When methin-[2-quinoline][3-(4-methyldihydro-2 : 4-benzthiazine)] (VI) was similarly heated with methyl sulphate, fusion did not occur. After heating at 120° for 2 hours, the product was converted into iodide (1·72 g. obtained). This was boiled out with methyl alcohol, leaving a sparingly soluble residue, and a 20% yield of dye crystallised from the filtrate. From m. p. and mixed m. p. determinations, it was concluded to be the same as the specimen prepared by the other method. It was also prepared from 3-methylthio-2 : 4-benzthiazine methiodide (1·69 g.), quinaldine methiodide, and triethylamine in alcohol. The crude, washed product (1·36 g.) was recrystallised from methyl alcohol (14 c.c.) and thus obtained in 33% yield (0·73 g.). M. p. 236° (decomp.), mixed m. p. with first specimen 227° (decomp.).

[2-(1-*Ethylquinoline*)][3-(4-*ethyl*-2 : 4-*benzthiazine*)]*methincyanine Iodide* (XII; R = Et).—Quinaldine ethiodide (1·5 g.) and 3-ethylthio-2 : 4-benzthiazine ethiodide were boiled and stirred together with triethylamine in ethyl alcohol for 4 minutes. The dye which crystallised on cooling was washed (1·43 g. obtained) and recrystallised from methyl alcohol (10 c.c. per g.), being obtained in 52% yield (1·24 g.) (Found: I, 26·75. $C_{22}H_{23}N_2IS$ requires I, 26·75%). The orange crystals had m. p. 212° (decomp.). The absorption maximum of their methyl-alcoholic solution was at 4625 A. with an inflexion at 4390 A. The dye was a weak sensitiser with the maximum effect at 4900 A., sensitisation extending to 5200.

[4-(1-*Ethylquinoline*)][3-(4-*ethyl*-2 : 4-*benzthiazine*)]*methincyanine Iodide* (XIII).—Lepidine ethiodide (2·99 g.) and 3-ethylthio-2 : 4-benzthiazine ethiodide were boiled and stirred with triethylamine in alcohol for 3 minutes. On addition of ether to the deep red solution, a red oil separated. Treatment with water converted it into a solid (2·95 g. obtained). After crystallisation from methyl alcohol (10 c.c. per g.), it was obtained in 45% yield (2·13 g.) (Found for material dried to constant weight in a vacuum at 70°: I, 26·8. $C_{23}H_{23}N_2IS$ requires I, 26·75%). The bright red needles had m. p. 95° (decomp.). The absorption maximum of a methyl-alcoholic solution was at 4955 A. It was a moderate sensitiser with the maximum at 5250 A., its action extending to 5600.

[2-(3-*Methyldihydro*-1 : 3-*thiazine*)][3-(4-*methyl*-2 : 4-*benzthiazine*)]*methincyanine Iodide* (XIV).—2-Methyldihydro-1 : 3-thiazine methiodide (2·0 g.) and 3-methylthio-2 : 4-benzthiazine methiodide were boiled and stirred with triethylamine in alcohol for 7 minutes. Addition of ether precipitated a yellow oil, which solidified on treatment with water. After crystallisation from methyl alcohol (15 c.c.), the yield was 11% (0·35 g.) (Found: I, 30·2. $C_{15}H_{19}N_2IS_2$ requires I, 30·35%). The yellow crystals had m. p. 235° (decomp.). The absorption maximum of a methyl-alcoholic solution was at 3790 A. The dye did not sensitise or depress blue sensitivity.

Methin-[2-(3-*ethyldihydrobenzthiazole*)][3-(2 : 4-*benzthiazine*)] *Hydriodide*.—2-Methylbenzthiazole (2·98 g.; 1 mol.), 3-ethylthio-2 : 4-benzthiazine (4·18 g.; 1 mol.), and ethyl *p*-toluenesulphonate (8 g.; 2 mols.) were heated together at 155—160° for 3 hours. The melt was dissolved in hot spirit (60 c.c.) and the crystals which separated on cooling were filtered off (5·62 g. obtained). They were dissolved in hot spirit and treated with a hot solution of potassium iodide (13·2 g.; 4 mols.) in water (40 c.c.). The resultant iodide (4·15 g.; 56% yield) was twice recrystallised from methyl

alcohol (160 c.c. per g.) and thus obtained in 38% yield (Found : I, 28·0. $C_{18}H_{17}N_3IS_2$ requires I, 28·05%). The golden-yellow crystals had m. p. 264—265° (decomp.). The methyl-alcoholic solution had its absorption maximum at 4090 in the presence of aqueous ammonia (5 c.c., *d* 0·880, per 100 c.c.) and at 4290 A. in the presence of sulphuric acid (5 g. per 100 c.c.). It was a strong sensitiser, sensitisation extending to 5000 A. with the maximum at 4600. This hydriodide (1 g.) was boiled and stirred for an hour with benzene (20 c.c.) and 10% sodium hydroxide solution (20 c.c.) : no solid was left undissolved. The benzene layer was washed and dried, and the solvent removed. The base was obtained in 88% yield (0·63 g.). Its m. p. and the mixed m. p. were identical with that of the specimen synthesised from 2-methylbenzthiazole etho-*p*-toluenesulphonate and 3-ethylthio-2 : 4-benzthiazine. The hydriodide was also prepared by adding a solution of the synthetic methin-[2-(3-ethyldihydrobenzthiazole)][3-(2 : 4-benzthiazine)] (3·24 g.; 1 mol.) in hot acetone (100 c.c.) to hydriodic acid (5·2 c.c.; *d* 1·5; 2 mols.) diluted with hot water. The iodide was filtered off, washed with water, and dried (4·63 g. obtained). On recrystallisation from methyl alcohol (180 c.c. per g.) it was obtained in 60% yield (2·71 g.) (Found : I, 28·15%). Its m. p. and absorption were identical with those of the other sample.

Methin-[2-(3-*ethyldihydro*-6 : 7-*benzbenzthiazole*)][3-(2 : 4-*benzthiazine*)] *Hydriodide*.—2-Methyl-6 : 7-benzbenzthiazole (1·99 g.), 3-ethylthio-2 : 4-benzthiazine, and ethyl *p*-toluenesulphonate were heated together at 150—160° for 4 hours. The hot melt was dissolved in hot absolute alcohol (10 c.c.) and treated with a hot solution of potassium iodide (3·3 g.) in water (20 c.c.). The dye was filtered off, washed, and ground with acetone (12 c.c.) (2·32 g. obtained; 46% yield). It was boiled out with methyl alcohol (20 c.c.), and the residue recrystallised from methyl alcohol (390 c.c. per g.). The yield of bright yellow crystals was 30% (1·51 g.) (Found : N, 5·55; I, 25·4; S, 12·7. $C_{23}H_{19}N_3IS_2$ requires N, 5·6; I, 25·3; S, 12·75%). M. p. 277° (decomp.). The absorption maximum of a methyl-alcoholic solution was at 4270 in the presence of alkali and at 4450 A. in the presence of acid. It was a powerful sensitiser with its maximum at 4700 A., the sensitisation extending to 5250. In a similar preparation where 3-ethylthio-2 : 4-benzthiazine was heated with ethyl *p*-toluenesulphonate for 2 hours, and the melt heated with 2-methyl-6 : 7-benzbenzthiazole etho-*p*-toluenesulphonate for a further 2 hours, the resultant dye iodide (42% yield) gave only a 9% yield of hydriodide on recrystallisation. When the melt from a preparation such as the first one was dissolved in alcohol and boiled and stirred for 10 minutes with triethylamine (1·2 mols.), the crude iodide (29% yield) again gave only a 9% yield of hydriodide.

Methin-[2-(3-*ethyldihydrobenzoxazole*)][3-(2 : 4-*benzthiazine*)] *Hydriodide*.—The crude, washed iodide (34% yield) from 2-methylbenzoxazole ethiodide, 3-ethylthio-2 : 4-benzthiazine, and ethyl *p*-toluenesulphonate, followed by potassium iodide, was recrystallised from methyl alcohol (80 c.c. per g.) and thus obtained in 25% yield (Found : N, 6·45; I, 29·2; S, 7·3. $C_{18}H_{17}ON_3IS_2$ requires N, 6·45; I, 29·1; S, 7·35%). The yellow crystals had m. p. 277° (decomp.) and their mixed m. p. with hydriodide which had been prepared from synthetic base was 277° (decomp.). The absorption maximum of a methyl-alcoholic solution was at 3840 in the presence of alkali and at 3970 A. in the presence of acid. The hydriodide was a moderate sensitiser with its maximum at 4300 A., and its action extended to 4550. This hydriodide was converted into base by the action of benzene and alkali and the conversion proceeded exactly like that of the hydriodide from synthetic base, giving a 36% yield of recrystallised base and a 12% yield of hydrochloride. In simultaneous m. p. determinations this and the synthetic base behaved similarly.

Methin-[2-(3-*ethyldihydro*-6 : 7-*benzbenzoxazole*)][3-(2 : 4-*benzthiazine*)] *Hydriodide*.—This was similarly prepared (42% crude yield) by use of 2-methyl-6 : 7-benzbenzoxazole (3·66 g.). After boiling out with methyl alcohol (20 c.c.) and then recrystallising from methyl alcohol (50 c.c. per g.) the yield was 24% (Found : N, 5·55; I, 26·4; S, 6·45. $C_{23}H_{19}ON_3IS$ requires N, 5·75; I, 26·1; S, 6·6%). The dye from the boiling out (7% yield) appeared to consist of a mixture of hydriodide and ethiodide (Found : I, 25·15. $C_{24}H_{23}ON_3IS$ requires I, 24·7%). The main crop of yellow hydriodide had m. p. 254° (decomp.). The absorption maximum of its methyl-alcoholic solution was at 3970 in the presence of alkali and at 4090 A. in the presence of acid. It was a powerful sensitiser with its maximum effect at 4500 A., its action extending to 5000. In an experiment where boiling and stirring with triethylamine (1·2 mols.) in alcohol was applied after the fusion, the yield of hydriodide after recrystallisation was 19% (Found : I, 25·95%).

Methin-[2-(3-*ethyldihydrobenzselenazole*)][3-(2 : 4-*benzthiazine*)] *Hydriodide*.—2-Methylbenzselenazole (1·96 g.), 3-ethylthio-2 : 4-benzthiazine, and ethyl *p*-toluenesulphonate were heated together, and the gum was dissolved in hot alcohol and treated with aqueous potassium iodide. The crystalline solid was filtered off, washed with water, and ground with acetone (15 c.c.) (53% yield obtained). It was boiled out with methyl alcohol (8 c.c.), and the residue recrystallised from methyl alcohol (300 c.c. per g.), giving a 29% yield (Found : N, 5·85; I, 25·9. $C_{18}H_{17}N_2ISSe$ requires N, 5·6; I, 25·4%). The bright yellow crystalline substance had m. p. 272° (decomp.) with previous darkening. The absorption maximum of a methyl-alcoholic solution was at 4100 in the presence of alkali and at 4350 A. in the presence of acid. It was a powerful sensitiser with its maximum at 4650 A., the action extending to 5200. When the melt in such a preparation was dissolved in alcohol and boiled and stirred with triethylamine or anhydrous potassium carbonate, unsatisfactory products were obtained in small amount.

5-3′-(4′-*Methyldihydro*-2′ : 4′-*benzthiazylidene*)-3-*ethylrhodanine* (XVII).—3-Methylthio-2 : 4-benzthiazine methiodide (1·69 g.; 1 mol.), 3-ethylrhodanine (0·81 g.; 1 mol.), anhydrous potassium carbonate (180-mesh; 0·35 g.; 0·5 mol.), and absolute alcohol (12 c.c.) were boiled and stirred together for 5 minutes. The washed product (1·05 g.) was recrystallised from methyl alcohol (310 c.c.) and thus obtained in 50% yield (0·81 g.) (Found : S, 30·05. $C_{14}H_{14}ON_4S_3$ requires S, 29·85%). The golden-yellow crystals had m. p. 190°. The narrow absorption band had its maximum at 4200 A. and an inflexion at 4000. It sensitised a chloride emulsion strongly with a sharp maximum at 4600 A., sensitisation extending to about 4900. It was also obtained by use of the salt which had been prepared from 3-methylthio-2 : 4-benzthiazine and ethyl iodide, and was obtained, after recrystallisation, in 43% yield. After a second recrystallisation the yield was 29% (Found : S, 29·8; N, 8·7. $C_{14}H_{14}ON_2S_3$ requires S, 29·85; N, 8·7%).

5-3′-(4′-*Methyldihydro*-2′ : 4′-*benzthiazylidene*)-4-*keto*-2-*thio*-3-*ethyltetrahydro-oxazole* (XVIII).—2-Methylthio-2 : 4-benzthiazine methiodide (1·69 g.; 1 mol.), 4-keto-2-thio-3-ethyltetrahydro-oxazole, and triethylamine (0·75 c.c.; 1·1 mols.) in ethyl alcohol were boiled together under reflux for 25 minutes. The product was filtered off, washed with water, dried (0·9 g. obtained), and recrystallised from methyl alcohol (60 c.c.), being obtained in 49% yield (0·75 g.). M. p. 167°. In another preparation the salt which had been prepared from 3-ethylthio-2 : 4-benzthiazine and methyl iodide was similarly heated with 4-keto-2-thio-3-ethyltetrahydro-oxazole and anhydrous potassium carbonate in alcohol. The water-washed product was recrystallised from methyl alcohol (80 c.c. per g.) and thus obtained in 42% yield (Found : S, 20·7. $C_{14}H_{14}O_2N_2S_3$ requires S, 20·95%). The lemon-yellow crystals had m. p. 169° and the mixed m. p. with the other sample was 168°. The absorption maximum of a methyl-alcoholic solution was at 3870 A. The compound sensitised a chloride emulsion strongly, with a maximum at 4100 A., the action extending to 4500.

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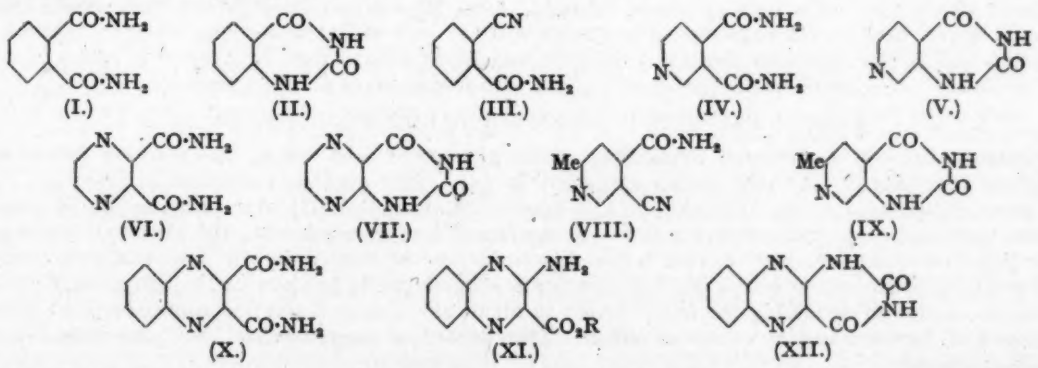
60. *The Application of the Hofmann Reaction to the Synthesis of Heterocyclic Compounds. Part I. Synthesis of Alloxazine from Quinoxaline-2 : 3-dicarboxylic Acid.*

By R. A. Baxter and F. S. Spring.

Quinoxaline-2 : 3-dicarboxylic acid is converted into *methyl quinoxaline-2 : 3-dicarboxylate* and thence into *quinoxaline-2 : 3-dicarboxyamide* (X). Treatment of this diamide with two molecular proportions of potassium hypobromite in excess of alkali yields alloxazine (XII) in 60% yield. When treated with one molecular proportion of potassium hypobromite in excess of alkali, the diamide (X) yields 2-aminoquinoxaline-3-carboxylic acid (XI, R = H) in 70% yield.

Various preparations of 2 : 4-dihydroxypyrimidine derivatives by the action of alkaline hypohalite solution upon 1 : 2-dicarboxyamides have been described in the literature.* The first example of the reaction was observed by Hoogewerff and van Dorp (*Rec. Trav. chim.*, 1891, **10**, 4; 1896, **15**, 107), who obtained 2 : 4-dihydroxyquinazoline (II) by the interaction of equimolecular proportions of potassium hypobromite and phthalamide (I) in alkaline solution. Similarly, cinchomeronamide (IV), when treated with two molecular proportions of potassium hypobromite in alkaline solution, gives a mixture of 3-aminopyridine-4-carboxylic acid and 2 : 4-dihydroxycopazoline (V) (Blumenfeld, *Monatsh.*, 1895, **16**, 702; Gabriel and Colman, *Ber.*, 1902, **25**, 2831). The general reaction has been applied to succinamide and *C*-substituted succinamides, which give dihydrouracil and substituted dihydrouracils respectively (Weidel and Roitner, *Monatsh.*, 1896, **17**, 174; van Dam, *Rec. Trav. chim.*, 1896, **15**, 101; McRae, Weston, and Hubbs, *Canadian J. Res.*, 1937, **15**, *B*, 434; McRae and McGinnis, *ibid.*, 1940, **18**, *B*, 90), to maleamide, which is thereby converted into uracil (Rinkes, *Rec. Trav. chim.*, 1927, **46**, 268), and to pyrazine-2 : 3-dicarboxyamide (VI), which yields 2 : 4-dihydroxypteridine (VII) (Gabriel and Sonn, *Ber.*, 1907, **40**, 4857). A variation of the general reaction is the conversion of *o*-cyanobenzamide (III) into 2 : 4-dihydroxyquinazoline (II) (Braun and Tcherniac, *Ber.*, 1907, **40**, 2709) and of 5-cyano-2-methyl*iso*nicotinamide (VIII) into 2 : 4-dihydroxy-6-methylcopazoline (IX) (Reider and Elderfield, *J. Org. Chem.*, 1942, **7**, 286).

This series of investigations was undertaken in order to examine the scope of the general reaction, more particularly to examine its application to the synthesis of condensed pyrimidine ring systems of the type present in certain naturally occurring products, and finally to examine obvious modifications of the general reaction with a view to the synthesis of heterocyclic systems other than pyrimidine. The present communication describes a synthesis of alloxazine (XII) by the action of alkaline potassium hypobromite upon quinoxaline-2 : 3-dicarboxyamide (X).



Methyl quinoxaline-2 : 3-dicarboxylate has been prepared by Ohle and Gross (*Ber.*, 1935, **68**, 2262) and the corresponding ethyl ester has been prepared by Chattaway and Humphrey (J., 1929, 645). Ohle and Gross obtained the methyl ester by condensing *o*-phenylenediamine with the crude product obtained by oxidation of methyl dihydroxymaleate with quinone, presumably a condensation of methyl diketosuccinate with *o*-phenylenediamine. According to these authors methyl quinoxaline-2 : 3-dicarboxylate has m. p. 325° and is insoluble in alcohol. Chattaway and Humphrey obtained the ethyl ester by direct esterification of quinoxaline-2 : 3-dicarboxylic acid and according to these authors it has m. p. 83° and is very easily soluble in alcohol. We attempted to prepare the ethyl ester by condensing *o*-phenylenediamine with ethyl diketosuccinate. The crude product was difficult to purify and after many crystallisations gave 2 : 3-dihydroxyquinoxaline. Many variations in the conditions employed for the condensation did not lead to the required ester. The condensation of ethyl 1-chloro-2-ketobutyrate with *o*-phenylenediamine was then examined in order to establish conditions for the direct synthesis of ethyl 2-methylquinoxaline-3-carboxylate, a reaction which involves oxidation and is analogous to a number of well-known pyrazine syntheses. It was hoped that a similar condensation of ethyl chloro-oxaloacetate with *o*-phenylenediamine would give ethyl quin-

* The corresponding reaction leading to the formation of 5-substituted hydantoins from *C*-substituted malonamides will be discussed in a later communication.

oxaline-2 : 3-dicarboxylate. In alcoholic solution ethyl 1-chloro-2-ketobutyrate and *o*-phenylenediamine gave a high yield of 2-methylbenziminazole hydrochloride. When the condensation was carried out in the presence of an aqueous suspension of calcium carbonate, the required ethyl 2-methylquinoxaline-3-carboxylate was obtained. The yield, however, was extremely low and the route was abandoned in favour of the successful one described below.

We next investigated the direct esterification of quinoxaline-2 : 3-dicarboxylic acid with methyl alcohol, this alcohol being chosen since in general methyl esters are amidated more easily than ethyl esters. *Methyl quinoxaline-2 : 3-dicarboxylate* was obtained in high yield, but the properties of this ester—m. p. 130°, easily soluble in alcohol—are markedly different from those of the product described under this name by Ohle and Gross. Methyl quinoxaline-2 : 3-dicarboxylate was characterised by hydrolysis to quinoxaline-2 : 3-dicarboxylic acid and by conversion into *quinoxaline-2 : 3-dicarboxyamide* (X), m. p. 328°, by treatment with methanolic ammonia.

Treatment of quinoxaline-2 : 3-dicarboxyamide with one molecular proportion of potassium hypobromite in alkaline solution gave 2-aminoquinoxaline-3-carboxylic acid (XI) in 70% yield. When treated with two molecular proportions of hypobromite in alkaline solution, however, the diamide gave alloxazine (XII) in similar yield; the alloxazine was characterised by conversion into its dimethyl derivative by treatment with diazomethane. The same remarkable difference in the course of the reaction between a dicarboxyamide and alkaline hypobromite solution according as one or two molecular proportions of the latter are employed has been previously observed in the case of pyrazine-2 : 3-dicarboxyamide by Gabriel and Sonn (*loc. cit.*) and confirmed in this laboratory by Mr. G. T. Newbold.

The conversion of a 1 : 2-dicarboxyamide into a 2 : 4-dihydroxypyrimidine derivative is an intramolecular application of the reaction whereby a monocarboxyamide is converted into an alkyl acylurea (Hofmann, *Ber.*, 1881, **14**, 2725; 1882, **15**, 407, 752, 762; Turpin, *Ber.*, 1888, **21**, 2488; Odenwald, *Annalen*, 1918, **416**, 228; 1919, **418**, 316) by successive treatment with bromine and alkali:

$$2R{\cdot}CO{\cdot}NH_2 + Br_2 + 2KOH \longrightarrow R{\cdot}CO{\cdot}NH{\cdot}CO{\cdot}NHR + 2KBr + 2H_2O \ (A).$$

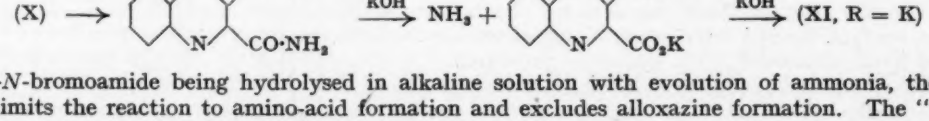
Applied to a dicarboxyamide, this reaction is expressed by the formula:

$$X\langle^{CO{\cdot}NH_2}_{CO{\cdot}NH_2} + Br_2 + 2KOH \longrightarrow X\langle^{CO-NH}_{NH{\cdot}CO} + 2KBr + 2H_2O$$

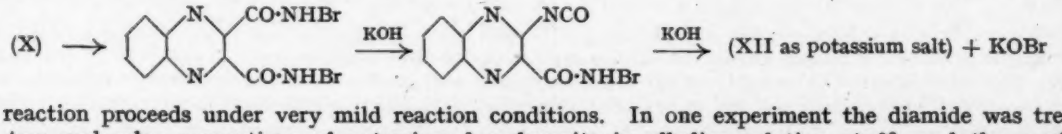
It has been assumed that the formation of an alkyl acylurea is to be attributed to the addition of acid amide to the intermediate *iso*cyanate (Hofmann, *loc. cit.*; see also Hoogewerff and van Dorp, *Rec. Trav. chim.*, 1896, **15**, 111; Graebe and Rostovzeff, *Ber.*, 1902, **35**, 2747), but this suggested mechanism cannot be considered satisfactory since Jeffreys (*Amer. Chem. J.*, 1899, **22**, 14) and Stieglitz and Earle (*ibid.*, 1903, **30**, 412) have shown that an *iso*cyanate does not react with an acid amide under conditions comparable with those employed in the Hofmann reaction. Stieglitz and Earle showed that an *iso*cyanate reacts vigorously with a *N*-halogen acid amide in the presence of alkali with formation of an alkyl acylurea:

$$R{\cdot}NCO + R{\cdot}CO{\cdot}NHBr + KOH \longrightarrow R{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}COR + KOBr$$

and assumed that the regenerated hypohalite reacts with more acid amide, the reaction proceeding to completion according to the proportions expressed in (*A*). This suggested mechanism offers an equally satisfactory explanation of the formation of 2 : 4-dihydroxyquinazoline (II) from phthalamide by treatment with one molecular proportion of hypohalite. A significant fact in considering the abnormal behaviour of quinoxaline-2 : 3-dicarboxyamide is that when this compound is treated in the cold with one molecular proportion of hypobromite in excess of alkali, ammonia is immediately produced, although no such evolution of ammonia occurs on dissolving the amide either in alkali alone or in a solution containing two molecular proportions of hypobromite in excess of alkali. This behaviour suggests that the "one mole" reaction proceeds as follows:



the mono-*N*-bromoamide being hydrolysed in alkaline solution with evolution of ammonia, the formation of which limits the reaction to amino-acid formation and excludes alloxazine formation. The "two mole" reaction is assumed to proceed by the steps:



This reaction proceeds under very mild reaction conditions. In one experiment the diamide was treated with two molecular proportions of potassium hypobromite in alkaline solution at 0°, and the resulting solution maintained at this temperature for 72 hours; the potassium salt of alloxazine had then separated in 60% yield. After removal of this salt the resulting solution contained only one-fifth of a mole of hypobromite. The explanation of this low hypobromite content was forthcoming when it was found that, after

a suspension of equimolecular proportions of alloxazine in alkaline potassium hypobromite solution had been maintained at 0° for 24 hours, the hypobromite content of the solution fell to half the original value.

Experimental.

2-Methylbenziminazole from o-Phenylenediamine and Ethyl 1-Chloro-2-ketobutyrate.—A solution of the ester (3·4 g.; 1/50 mol.) and the diamine (2·2 g.; 1/50 mol.) in absolute alcohol (10 c.c.) was refluxed for 3 hours. The residue obtained after evaporation (vacuum) of the mixture on the steam-bath was triturated with ether (50 c.c.). The solid product, which contained nitrogen and chlorine, was collected and washed with ether. It was very soluble in water and alcohol and insoluble in ether and benzene and did not melt below 300° (yield, 2·5 g.). This hydrochloride was dissolved in the minimum volume of water, and the base liberated by the addition of sodium hydroxide solution; 2-methylbenziminazole separated as needles, m. p. 173—175°, which after one recrystallisation from benzene–light petroleum attained the constant m. p. 175°, undepressed by an authentic specimen (Found: C, 72·3; H, 6·2. Calc. for $C_8H_8N_2$: C, 72·7; H, 6·1%).

Ethyl 2-Methylquinoxaline-3-carboxylate from o-Phenylenediamine and Ethyl 1-Chloro-2-ketobutyrate.—A mixture of the diamine (2·2 g.), the ester (3·4 g.), calcium carbonate (1 g.), and water (25 c.c.) was heated on the steam-bath for 8 hours. Carbon dioxide was slowly evolved. After standing overnight, the product crystallised. It was collected, washed with a little water, and recrystallised from hot water to give ethyl 2-methylquinoxaline-3-carboxylate as feathery needles, m. p. 72—73° (yield, 10%), which gave a negative halogen test. After sublimation at 60—70°/760 mm. the ester was obtained as long needles, m. p. 73°. Wahl and Doll (*Bull. Soc. chim.*, 1913, **13**, 468) give m. p. 73° for ethyl 2-methylquinoxaline-3-carboxylate obtained by condensation of *o*-phenylenediamine with ethyl diketobutyrate (Found: N, 13·4. Calc. for $C_{12}H_{12}O_2N_2$: N, 13·0%).

2 : 3-Dihydroxyquinoxaline from o-Phenylenediamine and Ethyl Diketosuccinate.—A solution of the ester (3·86 g.) in absolute alcohol (5 c.c.) was added to a warm solution of the diamine (2·2 g.) in absolute alcohol (10 c.c.). Reaction was instantaneous and proceeded with evolution of heat and the separation of a solid. When the reaction was complete the solid (3·5 g.) was collected and washed with alcohol. After repeated crystallisation from water it gave 2 : 3-dihydroxyquinoxaline as long needles not melting below 360°. It was freely soluble in dilute sodium hydroxide solution; its appearance and solubility properties were indistinguishable from those of an authentic specimen (Found: C, 59·05; H, 3·9; N, 17·7. Calc. for $C_8H_6O_2N_2$: C, 59·3; H, 3·7; N, 17·3%). The condensation was also effected (*a*) in benzene solution, (*b*) in aqueous suspension, and (*c*) in aqueous-alcoholic solution, in each case with the same result. Condensation of *o*-phenylenediamine and ethyl diketosuccinate under the conditions used by Wahl and Doll (*loc. cit.*) for the preparation of ethyl 2-methylquinoxaline-3-carboxylate from ethyl 1 : 2-diketobutyrate and *o*-phenylenediamine, also led to 2 : 3-dihydroxyquinoxaline.

Methyl Quinoxaline-2 : 3-dicarboxylate.—Quinoxaline-2 : 3-dicarboxylic acid was prepared by the method of Chattaway and Humphrey (*loc. cit.*); it had m. p. 190° (decomp.) and was characterised by conversion into the anhydride (yellow needles, m. p. 251°) by treatment with acetic anhydride. The acid (2 g.) was heated under reflux with methanolic hydrogen chloride (2%; 20 c.c.) for 2 hours. The solution was concentrated to half bulk (vacuum) and then poured into saturated sodium bicarbonate solution (20 c.c.). The ester was collected by filtration and purified by crystallisation from methanol, *methyl quinoxaline-2 : 3-dicarboxylate* (1·8 g.) separating as plates, m. p. 130° (Found: C, 58·7; H, 4·3; N, 11·2. $C_{12}H_{10}O_4N_2$ requires C, 58·5; H, 4·1; N, 11·4%). The methyl ester was converted into quinoxaline-2 : 3-dicarboxylic acid (m. p. and mixed m. p.) by heating with 10% aqueous potassium hydroxide solution for 1 hour on the water-bath, followed by acidification of the solution.

Quinoxaline-2 : 3-dicarboxyamide.—A solution of methyl quinoxaline-2 : 3-dicarboxylate (1·7 g.) in cold absolute methanol (70 c.c.) was saturated with dry ammonia. The product began to separate almost immediately and after standing overnight it was collected. After one recrystallisation from water the *diamide* separated as needles, m. p. 328° (decomp.) (yield, 93%) (Found: C, 55·6; H, 3·9. $C_{10}H_8O_2N_4$ requires C, 55·55; H, 3·7%).

2-Aminoquinoxaline-3-carboxylic Acid.—Quinoxaline-2 : 3-dicarboxyamide (1·08 g.) was dissolved with cooling in a mixture of water (14 c.c.) and potassium hypobromite solution (14 c.c.; 1 mol.); ammonia was immediately evolved. [The hypobromite solution used in this and the next experiment was prepared by adding bromine (16 g.) to aqueous potassium hydroxide solution (10%; 280 c.c.) at 0°. The hypobromite present was estimated by titration, and the solution found to contain 13·2 g. of potassium hypobromite.] The solution was kept at 0° overnight and then heated for 1 hour at 75—80°. No separation of solid had occurred at 0° after several hours. The clear solution was acidified with acetic acid, and the yellow solid collected, washed with water, and crystallised from aqueous acetic acid, 2-aminoquinoxaline-3-carboxylic acid separating as yellow needles, m. p. 212—213° (decomp.) either alone or when mixed with a specimen prepared by Mr. A. H. Gowenlock, using an unambiguous route to be described later (yield, 70%). Philips (*Ber.*, 1895, **28**, 1657) gives m. p. 210° (decomp.) for 2-aminoquinoxaline-3-carboxylic acid (Found: N, 22·4. Calc. for $C_9H_7O_2N_3$: N, 22·2%).

Alloxazine.—Quinoxaline-2 : 3-dicarboxyamide (1·08 g.) was dissolved at 0° in potassium hypobromite solution (28 c.c.; 2 mols.; see previous experiment) and maintained at this temperature overnight. The formation of ammonia could not be detected. The mixture was then maintained at 75—80° for 1 hour and cooled to 0°. After standing overnight, a heavy precipitate of the potassium salt of alloxazine had separated. This was collected, washed with ice-water (halogen test negative), dissolved in a minimum volume of hot water, and the solution acidified with acetic acid. The precipitated alloxazine was collected and combined with the material obtained by acidification of the mother-liquor from the potassium salt. It was purified by solution in aqueous sodium hydroxide (5%) and acidification of this solution with acetic acid. Alloxazine was obtained as a pale yellow powder which blackened above 300° but did not melt below 360° (yield, 60%) (Found: C, 55·8; H, 3·1; N, 26·2. Calc. for $C_{10}H_6O_2N_4$: C, 56·1; H, 2·8; N, 26·2%). A suspension of this product (0·15 g.) in dry ether (50 c.c.) was treated with an ethereal solution of diazomethane (from 2 c.c. of nitrosomethylurethane). The slow evolution of nitrogen was complete after standing overnight. The mixture was evaporated to dryness, and the residue washed with dilute sodium hydroxide solution and water and crystallised from alcohol to give 2 : 3-dimethylalloxazine as small yellow prisms, m. p. 236—237°, undepressed by a specimen prepared by methylation of authentic alloxazine; Kuhn and Bar (*Ber.*, 1934, **67**, 904) give m. p. 238° (corr.) for dimethylalloxazine (Found: C, 59·8; H, 4·4; N, 22·7. Calc. for $C_{12}H_{10}O_2N_4$: C, 59·5; H, 4·1; N, 23·1%).

The University, Manchester.

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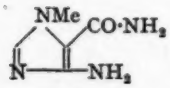
61. *The Application of the Hofmann Reaction to the Synthesis of Heterocyclic Compounds. Part II. Synthesis of Xanthine from Glyoxaline-4 : 5-dicarboxyamide and of 9-Methylxanthine from 1-Methylglyoxaline-4 : 5-dicarboxyamide.*

By R. A. Baxter and F. S. Spring.

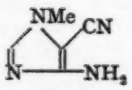
Glyoxaline-4 : 5-dicarboxylic acid is converted into *methyl glyoxaline-4 : 5-dicarboxylate* and thence into *glyoxaline-4 : 5-dicarboxyamide* (IV). Treatment of the last compound with alkaline potassium hypobromite solution gives xanthine (V), characterised by conversion into caffeine. When methyl glyoxaline-4 : 5-dicarboxylate reacts with sodium methoxide and methyl iodide, and the product is treated with alcoholic ammonia, *1-methylglyoxaline-4 : 5-dicarboxyamide* (VI) is obtained. The latter amide was also obtained by treatment of glyoxaline-4 : 5-dicarboxylic acid with diazomethane, followed by heating the product with alcoholic ammonia. By reaction with alkaline potassium hypobromite solution, 1-methylglyoxaline-4 : 5-dicarboxyamide (VI) yields 9-methylxanthine (VIII) (characterised by conversion into *iso*caffeine). This new synthesis of 9-methylxanthine is remarkable for the facility with which it proceeds, simple shaking of the diamide (VI) with alkaline hypobromite solution for 5 minutes at 0° leading to a separation of the potassium salt of 9-methylxanthine in a minimum yield of 60%. It is intended to apply this new purine synthesis to the preparation of a nucleoside of the xanthosine type.

Three different syntheses of purine derivatives have been accomplished starting from a glyoxaline derivative. Sarasin and Wegmann (*Helv. Chim. Acta*, 1924, **7**, 713) obtained 7-methylxanthine (heteroxanthine) in poor yield by treatment of 4-amino-1-methylglyoxaline-5-carboxyamide (I) (itself obtained by a four-stage route from 5-chloro-1-methylglyoxaline) with ethyl carbonate. Allsebrook, Gulland, and Story (J., 1942, 232) have shown that this method is probably applicable to the synthesis of 9-methylxanthine by the preparation of the intermediate 5-nitro-1-methylglyoxaline-4-carboxyamide. Montequi (*Anal. Soc. Fís. Quím.*, 1927, **25**, 182) obtained heteroxanthine in poor yield by treatment of 4-amino-5-cyano-1-methylglyoxaline (II) with urethane, followed by treatment of the product with hydrochloric acid. Finally, Allsebrook, Gulland, and Story (*loc. cit.*) obtained xanthine from 4(5)-ureidoglyoxaline-5(4)-carboxylic acid (III). These methods have the common feature that the correctly oriented glyoxaline derivative subjected to (pyrimidine) ring closure is in each case difficult of access.

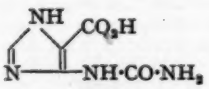
It appeared probable that application of the Hofmann reaction to the diamide of the readily available glyoxaline-4 : 5-dicarboxylic acid would give xanthine. This proved to be the case.



(I.)



(II.)



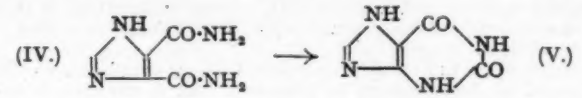
(III.)

It is reported (*Chem. Abs.*, 1934, **28**, 150) that Tamamushi prepared the ester (presumably the diethyl ester) and the acid chloride of glyoxaline-4 : 5-dicarboxylic acid. We have not had access to the original paper by Tamamushi and the abstract cited does not record the experimental conditions employed or the physical constants of the two derivatives. The same author has described ethyl 2-methylglyoxaline-4 : 5-dicarboxylate and ethyl 2-ethylglyoxaline-4 : 5-dicarboxylate and the two corresponding diamides (*J. Pharm. Soc. Japan*, 1935, **55**, 1053; 1937, **57**, 1023; 1938, **58**, 1).

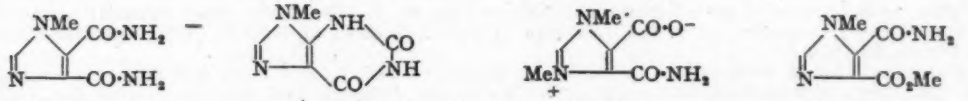
Preliminary experiments showed that glyoxaline-4 : 5-dicarboxylic acid gave intractable resinous material when treated with thionyl chloride, and esterification of the acid could not be accomplished under normal Fischer–Speier conditions. *Methyl glyoxaline-4 : 5-dicarboxylate* was, however, readily obtained in very high yield either by dissolving the acid in 100% sulphuric acid and pouring the solution into methanol (Newman, *J. Amer. Chem. Soc.*, 1941, **63**, 2431) or by refluxing a suspension of the acid in methanol saturated with hydrogen chloride. Methyl glyoxaline-4 : 5-dicarboxylate was readily converted into the corresponding *diamide* (IV), again in nearly quantitative yield. Treatment of glyoxaline-4 : 5-dicarboxyamide (IV) with potassium hypobromite in alkaline solution gave xanthine (V), characterised by conversion into caffeine. The course of this reaction does not appear to vary according as one or two molecular proportions of hypobromite are used, although in the former case the yield of xanthine is lower than in the latter.

Having established that the Hofmann reaction is applicable to glyoxaline-4 : 5-dicarboxyamide, a natural development was to apply the reaction to a 1-substituted glyoxaline-4 : 5-dicarboxyamide, which would be expected to yield either a 7- or a 9-substituted xanthine. To this end *1-methylglyoxaline-4 : 5-dicarboxyamide* (VI) was prepared by the reaction of methyl glyoxaline-4 : 5-dicarboxylate with sodium methoxide and methyl iodide, followed by treatment of the product with alcoholic ammonia. The diamide (VI) was also obtained by the action of diazomethane upon glyoxaline-4 : 5-dicarboxylic acid, followed by treatment of the product with alcoholic ammonia at 120°. If the product obtained by the action of diazomethane upon glyoxaline-4 : 5-dicarboxylic acid is treated with alcoholic ammonia at 0°, a *compound*, $C_7H_9O_3N_3$, m. p. 231° (decomp.), is obtained which is freely soluble in water but very sparingly soluble in alcohol. This compound, which is

probably either the betaine-amide (VII) or an amide-ester (*e.g.*, VII*a*), gives 1-methylglyoxaline-4 : 5-dicarboxyamide (VI) when heated with alcoholic ammonia at 120°.



(IV.) (V.)



(VI.) (VIII.) (VII.) (VII*a*.)

Treatment of the diamide (VI) with potassium hypobromite in alkaline solution gave 9-methylxanthine (VIII). The formation of 9-methylxanthine from 1-methylglyoxaline-4 : 5-dicarboxyamide is a remarkably facile reaction, simple shaking with potassium hypobromite solution for 5 minutes at 0° leading to the separation of the potassium salt of 9-methylxanthine in a minimum yield of 60%. The yield of 9-methylxanthine is greater than is the yield of xanthine from glyoxaline-1 : 2-dicarboxyamide, a fact which is probably attributable to the instability of xanthine in the presence of hypohalite solution (Biltz and Beck, *J. pr. Chem.*, 1928, **118**, 196), and to the relative insolubility of the potassium salt of 9-methylxanthine. 9-Methylxanthine was characterised by conversion into *iso*caffeine, m. p. 284—286°, which exhibited the characteristic absorption bands in the ultra-violet region of the spectrum with maxima at 2400 A. and 2675 A. (Gulland, Holiday, and Macrae, J., 1934, 1643).

This relatively simple preparation of a 9-substituted xanthine suggests a possible method for the synthesis of purine nucleosides of the xanthosine type, the successful development of which will require a method for the introduction of a suitable oriented glycosidic group at position 1 in glyoxaline-4 : 5-dicarboxyamide and, secondly, a sufficient degree of stability of this group under the alkaline conditions employed in the Hofmann reaction. Experiments designed to test this route are in progress.

Experimental.

Methyl Glyoxaline-4 : 5-dicarboxylate.—(*a*) Glyoxaline-4 : 5-dicarboxylic acid (*Org. Syn.*, **22**, 45) (2 g.) was dissolved in sulphuric acid (100%; 12 c.c.) with cooling, and the solution poured into dry methanol (50 c.c.). The mixture was refluxed for 15 minutes, solution then being complete. The alcohol was removed (reduced pressure), and the residue carefully diluted with water (200 c.c.). The solution was neutralised with calcium carbonate, filtered, and concentrated until crystallisation started. *Methyl glyoxaline-4 : 5-dicarboxylate* separated as rosettes of needles (1·7 g.), m. p. 198—200°, which after two recrystallisations from water had m. p. 200—203° (Found : C, 45·8; H, 4·4; N, 15·3. $C_7H_8O_4N_2$ requires C, 45·65; H, 4·3; N, 15·2%).

(*b*) Dry hydrogen chloride was passed into a suspension of glyoxaline-4 : 5-dicarboxylic acid (10 g.) in boiling methanol (100 c.c.) for 3 hours; solution was then complete. The solution was concentrated (reduced pressure) to 20 c.c. and poured into saturated aqueous sodium carbonate solution (50 c.c.). The separated solid was collected, washed with water, and recrystallised from water to give methyl glyoxaline-4 : 5-dicarboxylate as needles (9·8 g.), m. p. 200—202°, identical with the specimen obtained by method (*a*).

Glyoxaline-4 : 5-dicarboxyamide.—A solution of methyl glyoxaline-4 : 5-dicarboxylate (5 g.) in aqueous ammonia (*d* 0·88; 100 c.c.) was set aside at 20° for 14 hours. The *diamide* (4·2 g.) separated as needles which did not melt below 360°. It was but slightly soluble in water and alcohol. For analysis a specimen was recrystallised from much water (Found : C, 39·0; H, 3·9; N, 36·3. $C_5H_6O_2N_4$ requires C, 39·0; H, 3·9; N, 36·4%).

1-Methylglyoxaline-4 : 5-dicarboxyamide.—(*a*) A suspension of glyoxaline-4 : 5-dicarboxylic acid (3 g.) in ether (100 c.c.) was treated with an ethereal solution of diazomethane (from 10 c.c. of nitrosomethylurethane), nitrogen being evolved vigorously. After standing overnight, the ether was removed. The residual gum, which was very soluble in water and alcohol and insoluble in ether and benzene, could not be crystallised. It was dissolved in dry methanol (30 c.c.), a small quantity of unchanged acid removed by filtration, and the solution saturated with dry ammonia at 0°. This solution was heated at 120° in a sealed tube for 6 hours and evaporated to dryness. The residue crystallised from aqueous alcohol (charcoal) to give *1-methylglyoxaline-4 : 5-dicarboxyamide* as prisms (0·3 g.), m. p. 263—266° (decomp.) (Found : C, 42·5; H, 4·6; N, 33·8. $C_6H_8O_2N_4$ requires C, 42·9; H, 4·8; N, 33·3%).

The product obtained by treatment of glyoxaline-4 : 5-dicarboxylic acid (3 g.) with diazomethane as described above was dissolved in methanol, saturated with dry ammonia at 0°, and the solution left for 16 hours at room temperature. The crystalline product was collected and recrystallised from aqueous alcohol, from which the *compound* separated as needles (1·3 g.), m. p. 231° (decomp.) (Found : N, 23·4. $C_7H_9O_2N_3$ requires N, 23·0%). It was freely soluble in water and insoluble in alcohol and other common organic solvents. When heated with methanolic ammonia in a sealed tube at 120° for 6 hours, the compound $C_7H_9O_2N_3$ was converted into 1-methylglyoxaline-4 : 5-dicarboxyamide, m. p. and mixed m. p. 263—266°.

(*b*) A solution of methyl glyoxaline-4 : 5-dicarboxylate (4·6 g.) in dry methanol (200 c.c.) containing sodium methoxide (from 0·6 g. of sodium) was treated with methyl iodide (4·0 g.), and the mixture refluxed for 4 hours. The mixture was evaporated to half bulk, filtered, and the filtrate saturated with dry ammonia at 0°. On standing overnight, 1-methylglyoxaline-4 : 5-dicarboxyamide separated as prismatic needles (3·5 g.), m. p. 264—266° (decomp.), not depressed by the specimen described above.

Xanthine.—A solution of glyoxaline-4 : 5-dicarboxyamide (0·77 g.) in alkaline potassium hypobromite solution (28 c.c.; prepared as described on p. 231) was kept at 0° for 16 hours. The solution was heated on the steam-bath for 1 hour, cooled, and carefully acidified with acetic acid. The yellow precipitate was collected, washed with water, and digested with dilute aqueous ammonia (5·0 c.c., *d* 0·88, diluted with 20 c.c. of water). After removal of unchanged diamide (0·25 g.), the filtrate was heated to remove ammonia. On cooling, xanthine (0·15 g.) was deposited as flakes, not melting below 360°. A smaller yield of xanthine was obtained when the diamide was treated with one molecular

proportion of alkaline hypobromite solution. Analyses of xanthine prepared by this method were not satisfactory, since it was not possible completely to free it from inorganic material. Methylation of this product (100 mg.) by methyl sulphate and potassium hydroxide (Biltz and Beck, *J. pr. Chem.*, 1928, **118**, 198) gave caffeine (50 mg.), which separated from alcohol as feathery needles, m. p. 230—232°. After sublimation at 140°/10^{-3} mm., this had m. p. 231—232°, not depressed by an authentic specimen (m. p. 231—232°) (Found: C, 49·8; H, 5·3; N, 28·5. Calc. for $C_8H_{10}O_2N_4$: C, 49·5; H, 5·2; N, 28·9%).

9-*Methylxanthine*.—1-Methylglyoxaline-4 : 5-dicarboxyamide (0·85 g.) was shaken with alkaline potassium hypobromite solution (28 c.c., prepared as described on p. 231) at 0° for 5 minutes, a solid rapidly separating. The potassium salt was collected, washed with ice-water, and dissolved in the minimum volume of hot water. Acidification of this solution with acetic acid gave 9-methylxanthine (0·5 g.), m. p. 375—378°. After recrystallisation from much water, it was obtained as needles, m. p. 380° (decomp.) (Found: C, 43·7; H, 3·5; N, 33·6. Calc. for $C_6H_6O_2N_4$: C, 43·4; H, 3·6; N, 33·7%).

Light absorption. (*a*) In N/10-sodium hydroxide. Maxima at 2470 A., $\varepsilon = 8000$, and 2800 A., $\varepsilon = 8000$. Using a solution (pH, 10·0) of 9-methylxanthine in sodium hydroxide, Gulland, Holiday, and Macrae (*loc. cit.*) observed absorption maxima at 2470 A., $\varepsilon = 9300$, and at 2780 A., $\varepsilon = 9300$.

(*b*) In N/10-hydrochloric acid. Maxima at 2365 A., $\varepsilon = 6000$, and 2630 A., $\varepsilon = 8000$. Using a solution (pH, 5·0) of 9-methylxanthine in hydrochloric acid, Gulland, Holiday, and Macrae (*loc. cit.*) observed maxima at 2350 A., $\varepsilon = 7300$, and 2640 A., $\varepsilon = 9300$.

iso*Caffeine*.—9-Methylxanthine (100 mg.), prepared as described above, was suspended in dry ether (50 c.c.) and treated with an ethereal solution of diazomethane (from 2 c.c. of nitrosomethylurethane). Nitrogen was slowly evolved. After 3 days the mixture was evaporated, and the residue crystallised from alcohol, from which the product separated as small needles (55 mg.), m. p. 265—270°. After sublimation at 220°/10^{-3} mm., *iso*caffeine was obtained as a crystalline mass, m. p. 284—286°.* Biltz and Strufe (*Annalen*, 1921, **423**, 223) give m. p. 285—287° (corr.) for *iso*caffeine (Found: C, 49·7; H, 5·4; N, 28·4. Calc. for $C_8H_{10}O_2N_4$: C, 49·5; H, 5·2; N, 28·9%). *Light absorption in alcohol*: Maxima at 2400 A., $\varepsilon = 8400$, and 2675 A., $\varepsilon = 8300$. Gulland, Holiday, and Macrae (*loc. cit.*) observed maxima at 2400 A., $\varepsilon = 7600$, and 2690 A., $\varepsilon = 9000$ for a solution (pH, 10·0) of *iso*caffeine in sodium hydroxide.

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62. *Preparation and Properties of Sulphonacetamides: A Method for the Separation of Sulphonamides from N-Alkylsulphonamides.*

By H. T. OPENSHAW and F. S. SPRING.

A number of sulphonacetamides and *N*-alkylsulphonacetamides have been prepared. The determination of the titration equivalent of a sulphonacetamide gives a convenient method for the characterisation of the corresponding sulphonamide. A mixture of a sulphonamide and a *N*-alkylsulphonamide can be separated by acetylation and treatment of the resulting mixture with sodium bicarbonate solution, in which sulphonacetamides, but not *N*-alkylsulphonacetamides, are soluble. The acetyl groups can be removed subsequently by hydrolysis.

AROMATIC hydrocarbons and ethers, aryl chlorides and bromides are frequently identified by chlorosulphonation and subsequent conversion of the sulphonyl chloride into the corresponding sulphonamide (Huntress and Carten, *J. Amer. Chem. Soc.*, 1940, **62**, 511, 603; Huntress and Autenrieth, *ibid.*, 1941, **63**, 3446). A convenient and accurate method for the characterisation of sulphonamides and the estimation of their molecular weight has now been developed.

The small number of sulphonacetamides described in the literature were mostly prepared by boiling the corresponding sulphonamide with acetic anhydride for prolonged periods [D.R.-P. 466,519 (1929); Chaplin and Hunter, J., 1937, 1114; Jensen and Lundquist, *Dansk. Tids. Farm.*, 1940, **14**, 129; Kostsova, *J. Gen. Chem. Russia*, 1941, **11**, 63]. *o*-Nitrobenzenesulphonacetamide was obtained from the parent sulphonamide by the action of acetic anhydride and pyridine (Tozer and Smiles, J., 1938, 2052). Noelting (*Ber.*, 1875, **8**, 598) converted *p*-bromobenzenesulphonamide into its *N*-acetyl derivative by heating with acetyl chloride. The last method has the advantage of being very rapid and generally applicable. By this method seventeen sulphonacetamides have been prepared (Table I); of these, five have been previously described.

Chaplin and Hunter (*loc. cit.*) showed that toluene-*p*-sulphonacetamide decomposes carbonates and behaves as a monobasic acid when titrated against alkali with phenolphthalein as indicator. We likewise find that the sulphonacetamides shown in Table I are fairly strong acids (for toluene-*p*-sulphonacetamide, pK = 4·8 at 22·5°), and can readily be purified, since they are freely soluble in sodium bicarbonate solution. Furthermore they can be titrated against standard alkali with phenolphthalein as indicator. The observed and the calculated equivalents are shown in Table I.

The acidic properties of sulphonacetamides can be used to effect a separation of a sulphonamide from a *N*-alkylsulphonamide. Acetylation of such a mixture gives one of a sulphonacetamide and a *N*-alkylsulphonacetamide, of which only the former component is soluble in sodium bicarbonate solution. Sulphonacetamides and *N*-alkylsulphonacetamides are readily hydrolysed in alkaline solution, giving the corresponding sulphonamides and *N*-alkylsulphonamides respectively. A number of separations of this type have been effected. Of the *N*-alkylsulphonacetamides prepared by us, those which have not been described previously are listed in Table II.

* (*Note added in proof.*) A mixture of this with a sample of *iso*caffeine, m. p. 284—286°, kindly supplied by Professor J. M. Gulland, F.R.S., had m. p. 284—286°.

TABLE I.

Sulphonacetamides, $Ar{\cdot}SO_2{\cdot}NHAc$.

	Crystal form from aqueous alcohol.	M. p.	Formula.	N, %. Found.	N, %. Calc.	Equivalent. Found.	Equivalent. Calc.
Benzene-	Prismatic needles	124–125°	$C_8H_9O_3NS$	6·9	7·0	198; 198	199
Toluene-*p*-	Flattened needles	137 [1]	$C_9H_{11}O_3NS$	—	—	214; 213; 213	213
Toluene-α-	Needles	130 [2]	$C_9H_{11}O_3NS$	6·5	6·6	211; 213	213
p-Ethylbenzene-	Microcryst.	97	$C_{10}H_{13}O_3NS$	5·9	6·2	230	227
2 : 4 : 5-Trimethylbenzene-	Prisms	155	$C_{11}H_{15}O_3NS$	5·8	5·8	241	241
2 : 4 : 6-Trimethylbenzene-	Prismatic needles	165·5	$C_{11}H_{15}O_3NS$	5·9	5·8	241; 240	241
Naphthalene-1-	Large prisms	185	$C_{12}H_{11}O_3NS$	5·6	5·6	249; 248; 250	249
Naphthalene-2-	Small plates	145—146	$C_{12}H_{11}O_3NS$	5·6	5·6	249; 249	249
Tetralin-6-	Fine needles	138 [3]	$C_{12}H_{15}O_3NS$	5·3	5·5	255; 255	253
p-Cymene-?-	Laminæ	149	$C_{13}H_{17}O_3NS$	5·7	5·5	256; 256	255
p-Methoxybenzene-	Prisms	140	$C_9H_{11}O_4NS$	6·0	6·1	228; 230; 231	229
p-Ethoxybenzene-	Prismatic needles	151·5 [4]	$C_{10}H_{13}O_4NS$	5·7	5·8	244; 244	243
m-Nitrobenzene-	Small leaflets	189 [5]	$C_8H_8O_5N_2S$	11·6	11·5	244; 243	244
p-Nitrobenzene-	Prismatic needles	192 [6]	$C_8H_8O_5N_2S$	11·2	11·5	247; 244	244
p-Bromobenzene-	Leaflets	202—203 [7]	$C_8H_8O_3NBrS$	5·3	5·0	277; 278; 276	278
2 : 5-Dichlorobenzene-	Needles	214	$C_8H_7O_3NCl_2S$	5·2	5·2	270·5; 271	268
2 : 5-Dibromobenzene-	Prisms	228	$C_8H_7O_3NBr_2S$	3·7	3·9	354	357

[1] D.R.-P. 466,519 gives m. p. 139°. Hug, *Bull. Soc. chim.*, 1934, **1**, 990, gives m. p. 139; Chaplin and Hunter (*loc. cit.*) give m. p. 136—137°.
[2] Kostsova (*loc. cit.*) gives m. p. 129°.
[3] A mixture with the parent sulphonamide (m. p. 135°) melted at 117—119°.
[4] A mixture with the parent sulphonamide (m. p. 150°) melted at 132°.
[5] Jensen and Lundquist (*loc. cit.*) give m. p. 190—191°.
[6] Jensen and Lundquist (*loc. cit.*) give m. p. 192—193°.
[7] Noelting (*loc. cit.*) gives m.p . 202—203°.

TABLE II.

N-Alkylsulphonacetamides, $Ar{\cdot}SO_2{\cdot}NR{\cdot}COMe$.

Ar.	R.	Crystal form from aqueous alcohol.	M. p.	Formula.	N, %. Found.	N, %. Calc.
C_6H_5	$C_6H_5{\cdot}CH_2$	Prisms	76°	$C_{15}H_{15}O_3NS$	5·05	4·85
p-$CH_3{\cdot}C_6H_4$	$C_6H_5{\cdot}CH_2$	Laminæ	98	$C_{16}H_{17}O_3NS$	4·6	4·6
p-$C_6H_4{\cdot}Br$	CH_3	Flattened needles	94	$C_9H_{10}O_3NBrS$	4·9	4·8
p-$C_6H_4{\cdot}Br$	C_2H_5	Prisms	88·5—89·5	$C_{10}H_{12}O_3NBrS$	4·45	4·6
p-$C_6H_4{\cdot}Br$	$C_6H_5{\cdot}CH_2$	Small needles	88—89	$C_{15}H_{14}O_3NBrS$	3·9	3·8
m-$NO_2{\cdot}C_6H_4$	CH_3	Plates	132	$C_9H_{10}O_5N_2S$	10·9	10·85
m-$NO_2{\cdot}C_6H_4$	C_2H_5	Prismatic needles	89	$C_{10}H_{12}O_5N_2S$	10·65	10·3
β-$C_{10}H_7$	CH_3	Fine needles	82	$C_{13}H_{13}O_3NS$	5·5	5·3
β-$C_{10}H_7$	C_2H_5	Needles	76	$C_{14}H_{15}O_3NS$	5·2	5·05
β-$C_{10}H_7$	$C_6H_5{\cdot}CH_2$	Plates	168·5—169	$C_{19}H_{17}O_3NS$	3·9	4·1

Sulphonacetamides can be methylated by means of diazomethane to give the corresponding *N*-methylsulphonacetamide identical with that prepared by acetylation of the *N*-methylsulphonamide.

EXPERIMENTAL.

Sulphonacetamides.—The sulphonamide (1 part) was refluxed for 30 minutes with acetyl chloride (2½ parts): if solution was not complete in 5 minutes, glacial acetic acid (up to 2½ parts) was added. After removal of the excess of acetyl chloride, the cold reaction mixture was added to water, and the product collected, washed with water, and dissolved in warm sodium bicarbonate solution. The filtered solution was acidified with glacial acetic acid, and the sulphonacetamide crystallised from aqueous alcohol. The equivalent was determined by weighing accurately approximately 0·3 g. of the acetyl derivative, dissolving it in alcohol (50 c.c.; 50%), and titrating the solution against N/10-sodium hydroxide with phenolphthalein as indicator.

The dissociation constant of toluene-*p*-sulphonacetamide was estimated as follows: The amide (0·0020 mole) was dissolved in aqueous caustic soda (20·0 ml. of N/10, diluted to 50 ml.) by gentle warming, and the resulting solution cooled to room temperature (22·5°) and subjected to electrometric titration with N/10-hydrochloric acid, a "Cambridge" pH meter and a glass electrode being used. When 10·0 ml. of acid had been added, the solution had pH 4·79. The dissociation constant is thus approximately $1{\cdot}6 \times 10^{-5}$ at 22·5°.

N-Alkylsulphonacetamides.—The *N*-alkylsulphonamide was acetylated as described above. The reaction mixture was poured into water, and the product crystallised from aqueous alcohol. Separation of mixtures of a sulphonamide and a *N*-alkylsulphonamide was achieved as follows: The mixture was acetylated as described above. The cold reaction mixture was poured into water, and the product collected, washed with water, and digested with warm sodium bicarbonate solution. The insoluble *N*-alkylsulphonacetamide was collected and crystallised from aqueous alcohol. The alkaline filtrate was acidified with acetic acid, and the sulphonacetamide collected and crystallised from aqueous alcohol.

*Hydrolysis of Toluene-*p*-sulphonacetamide.*—The sulphonacetamide (2 g.) was refluxed with aqueous potassium hydroxide (5%; *ca.* 60 c.c.) for 1 hour. The cold solution was acidified with dilute hydrochloric acid, and the solid collected. A dried specimen had m. p. 135—136°. It was insoluble in sodium bicarbonate solution, and was undepressed in m. p. when mixed with authentic toluene-*p*-sulphonamide. The hydrolysis was also complete when the reaction period was reduced to 45 minutes, but when the reflux period was 30 minutes, 0·4 g. of unchanged toluene-*p*-sulphonacetamide (soluble in sodium bicarbonate) was recovered. Similar conditions led to the hydrolysis of naphthalene-1-sulphonacetamide.

N-Methyl-*p*-bromobenzenesulphonacetamide and *N*-methylnaphthalene-2-sulphonacetamide were hydrolysed by refluxing with 5% aqueous-alcoholic potassium hydroxide for 1 hour.

N-*Methyl*-p-*bromobenzenesulphonacetamide*.—A solution of *p*-bromobenzenesulphonacetamide (0·5 g.) in ether (60 c.c.) and methyl alcohol (10 c.c.) was treated with an ethereal solution of diazomethane. Reaction was instantaneous. The addition of the reagent was continued until the solution acquired a permanent yellow colour. After 1 hour the solution was evaporated to dryness, and the residue warmed with saturated sodium bicarbonate solution. The insoluble oil was separated; it solidified on trituration with cold water. Crystallisation from aqueous alcohol gave *N*-methyl-*p*-bromobenzenesulphonacetamide as sword-like needles, m. p. 94°, undepressed when mixed with a specimen prepared by acetylation of *N*-methyl-*p*-bromobenzenesulphonamide. Similar treatment of naphthalene-2-sulphonacetamide and of toluene-*p*-sulphonacetamide gave respectively *N*-methylnaphthalene-2-sulphonacetamide (needles from aqueous alcohol, m. p. 82°, undepressed when mixed with a specimen prepared by acetylation of *N*-methylnaphthalene-2-sulphonamide) and *N*-methyltoluene-*p*-sulphonacetamide [prisms from aqueous alcohol, m. p. 59°, undepressed when mixed with the specimen obtained by acetylation of *N*-methyltoluene-*p*-sulphonamide (Chaplin and Hunter, *loc. cit.*)].

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63. *Molecular Volume and Structure. Part IX.*

By T. W. GIBLING.

The recent publication of new determinations of parachors of a number of paraffins affords an opportunity to review the method of calculation previously proposed. Visualisation of a molecular volume as consisting in general of the " spheres of influence " of the constituent atoms—these " spheres " always interpenetrating to some extent—confirms the idea that the method of derivation of " atomic and structural constants " was based on mistaken assumptions; it also gives a simple explanation of the reductions in parachor value observable in all homologous series, these reductions being produced by " interference " between non-linked atoms, *i.e.*, by the overlapping of their " envelope volumes " or " spheres of influence."

QUAYLE, DAY, and BROWN (*J. Amer. Chem. Soc.*, **1944**, **66**, 938) state that " the parachors in *n*-saturated hydrocarbons have been found to be almost unique in being additive in nature," though they modify this in a footnote: " Even the values for the saturated hydrocarbons are not considered to be strictly additive by some observers. However, they are at least essentially so. If variations exist they appear to be of a distinctly lower order of magnitude for chains of short or moderate length." They add: " It is essential that the CH_2 increment in the saturated hydrocarbons be re-examined from time to time as compounds of higher purity become available and as the techniques of measurement are improved," and they determined the parachors of eight *n*-paraffins, pentane to duodecane, concluding that " there is no apparent change in the CH_2 increment as the chain is increased up to $C_{12}H_{26}$," their mean CH_2 values (over the temperature range 20—50°) varying from 39·5 to 40·5, with an over-all mean of 40·0.

These statements are in accord with the ideas expressed by the author in discussing the methods used in the calculation of parachors (J., 1941, 299), in reference to which Quayle *et al.* quote him correctly as asserting " that the CH_2 value seems to show progressively higher values throughout any homologous series," but incorrectly as saying that this is " due to decreasing ' interference ' effects." No hypothesis was advanced by the author to account for the so-called " expansion " phenomenon (for the existence of which he adduced evidence from the parachors of more than 20 compounds of high molecular weight), but it was later suggested by him that among the lower members of any series other than the *n*-paraffins " interference " effects might be expected, which would produce irregularities in the progression in the case of the earlier CH_2 increments.

The formula proposed by the author to represent the parachors so far recorded for *n*-paraffins was $[2c + (n - 2)k]f^n$, where c, the value for $CH_3{-}$, was 55·2; k, the $-CH_2-$ value, was 39·8; f 1·0004165, and n the number of carbon atoms in the molecule. According to this, the CH_2 difference, starting at 39·9 for $n = 2$ or 3, would become 40·2 for $n = 10$ or 11; for $n = 2$—12, the mean CH_2 difference would be rather more than 40·0; for $n = 59$ or 60, it would be 41·8, with a mean of rather less than 40·9 between $n = 2$ and 60. Inclusion of the newly determined parachors gives a slightly improved agreement between calculated and mean observed values as compared with that shown in the original table (*loc. cit.*, p. 301), as follows:

n-Paraffins, C_nH_{2n+2}.

n.	[*P*], calc.	[*P*], obs.†	Diff., %.	*n*.	[*P*], calc.	[*P*], obs.†	Diff., %.	*n*.	[*P*], calc.	[*P*], obs.†	Diff., %.
2	110·5	110·5	±0·0	7	310·3	310·1[3]	−0·1	12	510·9	510·6	−0·1
3	150·4	150·8	+0·3	8	350·4	350·8[3]	+0·1	26	1077	1082	+0·5
4	190·3	190·3	±0·0	9	390·5	391·1	+0·2	32	1322	1322	±0·0
5	230·3	231·0	+0·3	10	430·6	430·5[2]	−0·0	60	2480	2480	±0·0
6	270·3	270·6[4]*	+0·1	11	470·8	470·8	±0·0				

* Excluding one determination (273·3) which differs from the rest by 1%.

† The figure in brackets gives the number of independent observations upon which the mean [*P*] value is based.

The mean difference (col. 4) is just over ± 0·1%, and the better agreement between observed and calculated values for high molecular-weight compounds obtained by using the author's formula is illustrated, for the last

three paraffins, by comparison of the observed values with those calculated from the constants proposed by various workers: Sugden (S), Mumford and Phillips (MP), Vogel (V), Desreux (D), Bayliss (B), Quayle *et al.* (Q). The last two columns in the following table contain the values calculated by the author (G) and the observed values.

Atom, group, etc.	(S).	(MP).	(V).	(D).*	(B).†	(Q).	(G).	Obs.
C	4·8	9·2	11·5	8·3	9·1	9·0	—	—
H	17·1	15·4	14·4	15·8	15·4	15·5	—	—
CH_3–	56·1	55·4	54·7	55·7	55·3	55·5	55·2 ‡	—
–CH_2–	39·0	40·0	40·3	39·9	39·9	40·0	39·8 ‡	—
n-$C_{16}H_{34}$	1048	1071	1077	1069	1068	1071	1077	1082
n-$C_{22}H_{46}$	1282	1311	1318	1308	1308	1311	1322	1322
n-$C_{60}H_{122}$	2374	2431	2447	2426	2425	2431	2480	2480
Mean diff., %	3·6	1·4	0·7	1·5	1·6	1·4	0·2	—

* *Bull. Soc. chim. Belg.*, 1935, **44**, 249. † *J. Amer. Chem. Soc.*, 1937, **59**, 444.
‡ "Reduced parachor" values—see later.

The percentage differences on which the above means are calculated are those between $[P]$, obs. and $[P]$, calc. For the whole 14 paraffins, the respective mean percentage differences are: ± 1·6, 0·3, 0·4, 0·5, 0·5, and 0·4, as compared with the author's ± 0·1, mentioned above.

The eight new values measured by Quayle *et al.* are on the average about 0·1% higher than those calculated by the author's formula, but before any change is made in the constants in that formula, it would appear advisable to determine afresh the parachors of the last three hydrocarbons in the above table and of others between, say, C_{20} and C_{60}.

In their calculations, most observers continue to use values, styled "atomic constants," like those quoted above for C and H. As previously explained (*loc. cit.*), the author regards the method by which such values have been obtained as inadmissible for two reasons: (1) the volume contribution of any atom, such as C, is not constant but varies according to the nature of the other atoms with which it is linked; (2) no allowance has been made for the "interference" between the non-linked atoms in the grouping $\gtrless C{\cdot}CH_2{\cdot}C \lessgtr$. In each case the effective contribution of C in $-CH_2-$ is reduced in comparison with that of C in $-CH_3$.

The above argument will become clearer if one considers the nature of a "molecular volume." That of neon at its b. p., *i.e.*, − 246·3°, is 16·8, giving $27{\cdot}7 \times 10^{-24}$ cm.^{3} as the mean volume of a neon atom at that temperature. This volume may be regarded ideally as a sphere of radius $1{\cdot}88 \times 10^{-8}$ cm., consisting of an "envelope volume" surrounding the much smaller sphere which may be considered to represent the normal confines of the atom (Fig. 1). The extent of this envelope will depend upon the conditions, increasing, *e.g.*, with rise in temperature. Now the parachor of a liquid is regarded as a "comparative volume" in such ideal conditions that the liquid is under standard internal pressure. Thus, the ideal volumes of an atom of, say, neon ($[P]$, 25·0) and one of argon ($[P]$, 54·0) may be visualised as spheres with volumes proportional to these numbers.

Pauling ("The Nature of the Chemical Bond," 1940, 164) lists the following covalent radii (in A.) for atoms of some of the earlier elements:

H.	He ($[P]$, 20·5).	C.	N.	O.	F.	Ne ($[P]$, 25·0).
0·30	—	0·77	0·70	0·66	0·64	—

If now one imagines the atoms C to F in their simple hydrides with the hydrogen atoms stripped off, but the atom still retaining all the outer electrons, one has the four negative ions each with the same electronic structure as $:\ddot{\underset{\ddot{}}{\text{Ne}}}:$. The ideal volumes of this series of atoms should then be in descending order of magnitude, with the volume of C probably rather more than twice that of Ne. Consider now two similar atoms covalently linked by a single bond, as in F_2 or $:\ddot{\underset{\ddot{}}{\text{F}}}:\ddot{\underset{\ddot{}}{\text{F}}}:$. The "envelope volumes" of the two atoms will interpenetrate to some extent, as illustrated, with rather extreme simplification, in Fig. 2, and thus the molecular volume of F_2 will be less than twice the ideal volume of $:\ddot{\underset{\ddot{}}{\text{F}}}:$. Similar diagrams would serve to illustrate the molecular volumes of $H:H$ and $:\ddot{\underset{\ddot{}}{\text{C}}}:\ddot{\underset{\ddot{}}{\text{C}}}:$ (as in $CH_3{\cdot}CH_3$). If two atoms of different size are linked, *e.g.*, $:\ddot{\underset{\ddot{}}{\text{C}}}:H$, the result will be as shown in Fig. 3, with the effective volumes of the C and H atoms (indicated by using a dotted line as the section of the circular internal boundary), respectively greater and less than they would be in C–C and H–H.

Now consider the linkage of three carbon atoms as in Fig. 4: a further decrease in volume would appear likely to be brought about by the overlap of the "envelope volumes," or "spheres of influence," of the non-linked atoms C_1 and C_3, as indicated in the darkened part of the figure. The evidence for such a decrease in volume is given by the values calculable for the groups existing in paraffins, *n*-, *iso*-, and *neo*-. On the author's scale of "reduced parachors" (R.P.)—a term preferable to "standard values" (*loc. cit.*, p. 302; J., 1943, 150)—the following R.P.'s form a series with the differences between adjacent members not constant, as might have been expected, but with a constant increase of 2·2 units: CH_4, 68·4; $CH_3{\cdot}(C)$, 55·2 (diff., 13·2); $(C){\cdot}CH_2{\cdot}(C)$, 39·8 (diff., 15·4); $\begin{matrix}(C)\\(C)\end{matrix}\!\!>\!CH{\cdot}(C)$, 22·2 (diff., 17·6); $\begin{matrix}(C)\\(C)\end{matrix}\!\!>\!C\!<\!\!\begin{matrix}(C)\\(C)\end{matrix}$, 2·4 (diff., 19·8). This constant increase is

attributed by the author to "interference" between atoms attached to a common carbon atom. Thus, let the reductions in R.P. value due to the various groupings be as follows: $C\langle C \rangle$, a; $C\langle \overset{C}{H} \rangle$, b; $C\langle \overset{H}{H} \rangle$, c. Then, we have the following scheme:

Group.	Reductions.	Diff.	Const. diff. of differences.
CH_4	$6c$	—	—
$CH_3\cdot(C)$	$3b + 3c$	$3b - 3c$	—
$(C)\cdot CH_4\cdot(C)$	$a + 4b + c$	$a + b - 2c$	$a - 2b + c$
$(C)_2CH\cdot(C)$	$3a + 3b$	$2a - b - c$	$a - 2b + c$
$(C)_2C(C)_2$	$6a$	$3a - 3b$	$a - 2b + c$

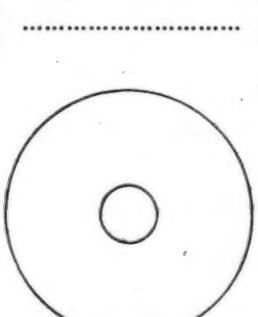


FIG. 1.

FIG. 2.

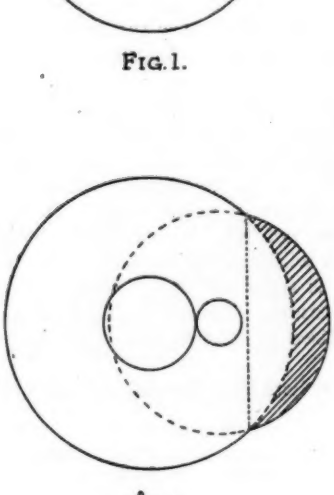


FIG. 3.

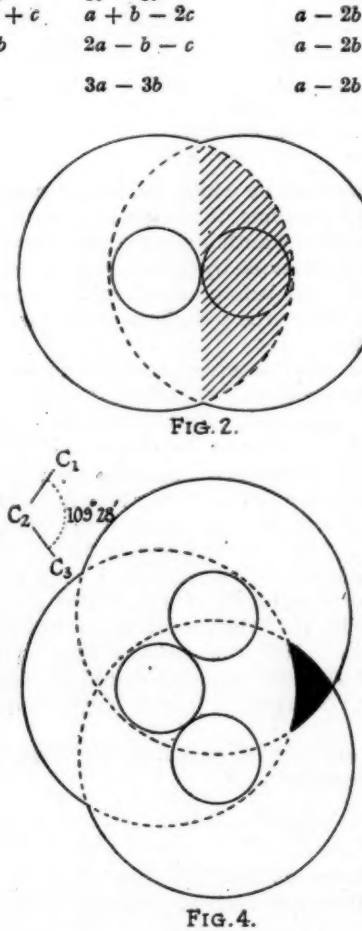


FIG. 4.

It has been assumed, apparently with justification, that b and c are negligible, whence $a = 2{\cdot}2$; but if this is not so, then most probably a is rather greater (*e.g.*, if, say, $b = 0{\cdot}3$ and $c = 0{\cdot}1$, then $a = 2{\cdot}7$).

The method, adopted by Sugden ("The Parachor and Valency," 1929, 35) and followed by later investigators, for the calculation of "atomic constants" consists essentially in subtracting the CH_2 value from the CH_3 value to give the value of H. If we also followed this method, using the CH_3 and CH_2 values given above, we should obtain H, 15·4; C, 9·0. According to the preceding argument, however, the CH_2 value has been decreased by 2·2, owing to "interference," and should therefore be reckoned as 42·0, whence H, 13·2; C, 15·6. These values would, of course, give satisfactory results in calculations, providing that the necessary corrections for interference occurring in carbon chains were made; but what exactly do these values so calculated for H and C stand for? The answer to this question can be found from a consideration of Figs. 2 and 3. The value for H (13·2), which may conveniently be abbreviated as [H], is equal to $\left[H-\overset{H}{\underset{H}{C}}-(C)-(C)-\overset{H}{\underset{H}{C}}-(C)\right]^{*} = 55{\cdot}2 -$ 42·0. Now, $\left[H-\overset{H}{\underset{H}{C}}-(C)\right] = \left[:\ddot{C}: + 3h - c/2\right]$, where h is $\left[:\ddot{C}:H - :\ddot{C}:\right]$, as in the shaded portion of Fig. 3, and $c/2$ is half the loss in volume due to the linkage of two carbon atoms, as in the shaded part of

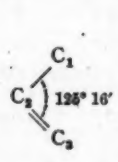
* Both these groups are assumed to be free from interference—see Part I, *loc. cit.*, p. 302.

Fig. 2; while $\left[\begin{array}{c}H\\|\\(C)—C—(C)\\|\\H\end{array}\right] = \left[\begin{array}{c}\cdot\cdot\\:\dot{C}:\\\cdot\cdot\end{array} + 2h - c\right]$. Thus $[H] = [h + c/2]$; *i.e.*, the value allotted to H depends to a great extent upon the volume reduction produced by a C—C linkage. By similar argument one derives the value for C (15·6) as $\left[\begin{array}{c}(C)\\(C)\end{array}\!\!>\!C\!<\!\!\begin{array}{c}(C)\\(C)\end{array}\right]^*$, *i.e.*, $\left[\begin{array}{c}\cdot\cdot\\:\dot{C}:\\\cdot\cdot\end{array} - 2c\right]$.

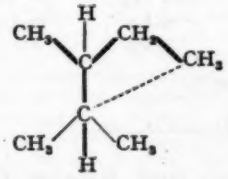
Using Sugden's method for calculating " structural constants," we should obtain + 15·4 as the value for a double bond (R.P., C_2H_4, 99·4; *loc. cit.*), and by reasoning similar to the above, this value can be shown to represent [2 volume reductions for a C—C linkage]—[the volume reduction due to a C=C linkage]. Since the carbon atoms in C=C are more closely associated than those in C—C, the reduction in volume for the former linkage will presumably be rather greater than that for the latter, but this is more than compensated for by the smaller number of carbon-to-carbon linkages in the molecule in the former case; which accounts for the *positive* value of the " double-bond constant." The double-bond group values derived from the R.P. of olefins, *viz.*, CH_2=(C), 49·7; (C)·CH=(C), 34·3; $\begin{array}{c}(C)\\(C)\end{array}\!\!>\!C=(C)$, 16·7, form a series with differences 15·4 and 17·6, *i.e.*, increasing by 2·2. Hence interference between C_1 and C_3 in the grouping (I) appears to be about the same as that between the corresponding atoms in Fig. 4, involving a correction of − 2·2 in each case. This seems reasonable from a calculation of the distance between C_1 and C_3 in each: the distances C—C and C=C being taken as 1·54$_2$ and 1·33 A., respectively, those between C_1 and C_3 in Fig. 4 and (I) are 2·52 and 2·55 A., respectively.

Quayle *et al.* (*loc. cit.*) also record the parachors of 18 *iso*-paraffins, 5 from their own measurements, and they conclude that the effect of branching of the carbon chain is not uniform, but that decreases in volume become greater as the branch moves towards the centre of the chain and as the length of the branch is increased. Except for those having one or other of two special types of structure, *iso*- and *neo*-paraffins so far investigated continue to show reasonable agreement between mean observed parachors and those calculated from the group values recorded above. In the following table, expansion corrections (E.C.) are taken from the table in Part I (*loc. cit.*, p. 304), in which lists of values for R.P. (or S.V.), [*P*], and E.C. (as the difference between the preceding two values) are given for all *n*-paraffins from ethane to hexacontane—the rate of expansion appears to be the same in all series, depending only upon the magnitude of the parachors. The reduced parachors are found to be truly additive and constitutive functions within the limits of experimental error.

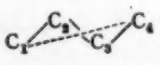
Paraffin.	R.P., calc.	E.C.	[*P*], calc.	[*P*], obs.	Diff., %.
2-Methylbutane	227·6	+0·5	228·1	230·0	+0·8
3-Methylpentane	267·4	+0·7	268·1	267·9	−0·1
2 : 2 : 3-Trimethylbutane	300·6	+0·8	301·4	301·4	±0·0
2 : 2-Dimethylpentane	302·8	+0·9	303·7	305·3	+0·5
2 : 4-Dimethylpentane	305·0	+0·9	305·9	306·5[2]	+0·2
2-Methylhexane	307·2	+0·9	308·1	309·1	+0·3
3-Methylhexane	307·2	+0·9	308·1	306·85[2]	−0·4
2 : 4-Dimethylhexane	344·8	+1·1	345·9	344·9	−0·3
2 : 5-Dimethylhexane	344·8	+1·1	345·9	345·9[3]	±0·0
2-Methylheptane	347·0	+1·2	348·2	349·05[2]	+0·2
3-Methylheptane	347·0	+1·2	348·2	347·7	−0·1
4-Methylheptane	347·0	+1·2	348·2	347·6	−0·2
2 : 4-Dimethylheptane	384·6	+1·4	386·0	381·1	−1·3
2 : 5-Dimethylheptane	384·6	+1·4	386·0	384·9	−0·3
2 : 7-Dimethyloctane	424·4	+1·8	426·2	425·9[5]	−0·1



(I.)



(II.)

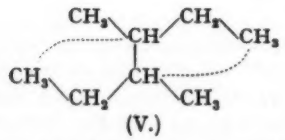


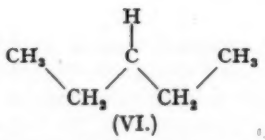
(III.)

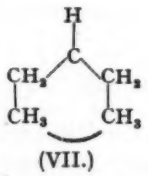
(IV.)

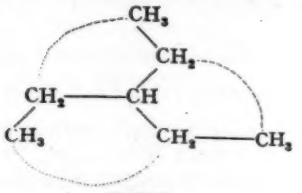
One type of *iso*-paraffin for which the parachor, as calculated by the above method, is consistently higher than the observed value is that containing two adjacent >CH groups to one or both of which is attached an ethyl, or higher, radical, *e.g.*, 2 : 3-dimethylpentane (II). It seems likely that the most stable configuration of the groups in this molecule will be as shown here, the top and the bottom portion occupying *cis-trans*-positions. Then the $-CH_2$ of the ethyl group, tending to be repelled by the other CH_3 groups, will probably take up a position in which there is mutual interference between it and the further >CH group. Now the distance between C_1 and C_4 in (III) is 3·89 A. and in (IV) 2·57 A., all four atoms lying in the same plane in each case. For the distance 2·52 A. between two non-linked carbon atoms, the parachor " interference correction " is − 2·2 (see above), whereas for the distance 3·89 A. the correction must be negligible (otherwise the R.P. increment between C_2H_6 and C_3H_8 would be greater than that for successive pairs of *n*-paraffins). For the distance 2·57 A.,

then, one might expect a negative correction rather less than 2·2; actually it is — *1·7*. [It does not necessarily follow, of course, that all the four carbon atoms, as shown in this molecule (II), are in exactly the same plane.]


(V.)


(VI.)


(VII.)


(VIII.)

The full method of calculation for the parachor of a substance is illustrated in the case of 3 : 4-dimethylhexane (V), in which the upper and the lower half of the molecule are regarded as being in *cis-trans*-positions. From the sum of the group values (which themselves usually involve corrections for interference) is taken the sum of any extra corrections; this gives the "reduced parachor" (R.P.) (see p. 237). To this is then added the "expansion correction" (E.C.) and the result is the theoretical parachor, which in most cases is found to be approximately equal to that determined by experiment. Thus:

4 CH_2·(C) at 55·2	220·8	2 corrns. at −1·7 (see above)	−3·4
2(C)·CH_2·(C) at 39·8	79·6	Reduced parachor (R.P.)	341·4
2 $\begin{matrix}(C)\\(C)\end{matrix}\!>$CH·(C) at 22·2	44·4	Expansion correction (E.C.)	+1·1
Σ group values	344·8	Parachor calculated	342·5

Paraffin.	R.P., calc.	E.C.	[*P*], calc.	[*P*], obs.	Diff., %.	Extra corrns. (as above).
2 : 3-Dimethylpentane	303·3	+0·9	304·2	304·3	+0·0	−1·7
3 : 4-Dimethylhexane	341·4	+1·1	342·5	342·6	+0·0	−3·4
2 : 3-Dimethylhexane	343·1	+1·1	344·2	344·1	−0·0	−1·7
2 : 3-Dimethylheptane	382·9	+1·4	384·3	373·1	−2·9	−1·7

It will be observed that in the above two tables two *iso*-paraffins, *viz.*, 2 : 3- and 2 : 4-dimethylheptane, show very poor agreement between calculated and observed parachors.

3-Ethyl-pentane and -hexane each appear to require extra corrections of about — 3·6. These hydrocarbons may be regarded as symmetrically trisubstituted derivatives of trimethylmethane, the structure of which is obvious. In triethylmethane (3-ethylpentane) it would appear that each of the additional carbon atoms produces inteference necessitating a correction of — *1·2*, this interference occurring between all the three CH_3 groups or between each of them and the nearer of the other CH_2 groups in each case. It is clear that in 3-ethylpentane the CH_3 groups cannot be in either of the extreme positions shown in (VI) and (VII), in which they are imagined as being in a plane respectively above and below that of the CH_2 groups. In the former case the carbon-to-carbon distance would obviously be too great for interference; in the latter, the distances between the CH_3 groups would be 2·52 A., and the interference correction for each pair would be — 2·2, making a total correction of — 6·6. The CH_3 groups therefore appear to take up some intermediate position, such as that in (VIII), in which all the six carbon atoms of the CH_2 and CH_3 groups are shown as approximately in the same plane. If they are actually coplanar, the distance between the carbon of each CH_3 group and the carbon of the nearer (unlinked) CH_2 group will be 2·73 A. In (VIII) the molecule is shown as viewed from above; in (VI) and (VII), a side view of part of the molecule is given.

Paraffin.	R.P., calc.	E.C.	[*P*], calc.	[*P*], obs.	Diff., %.	Extra corrns. (as above).
3-Ethylpentane	303·6	+0·9	304·5	304·2	−0·1	−3·6
3-Ethylhexane	343·4	+1·1	344·5	345·0	+0·1	−3·6

THE GRAMMAR SCHOOAL OF QUEEN ELIZABETH, WAKEFIELD. [*Received, January 4th*, 1945.]

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64. p-*Sulphonamidobenzylaniline and Related Compounds of Pharmacological Interest.*

By W. KELLY, T. D. ROBSON, and W. F. SHORT.

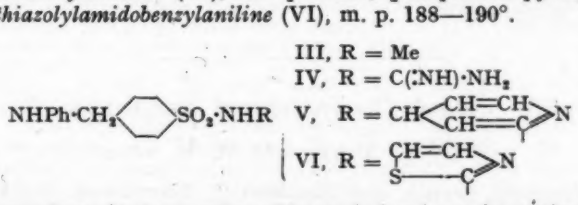
Chlorosulphonation of acetobenzylanilide affords aceto-*p*-chlorosulphonylbenzylanilide and its *m*-isomer in the approximate ratio 4 : 1. A number of compounds of the marfanil type have been prepared by condensing the *p*-sulphonyl chloride with ammonia, methylamine, guanidine, 2-aminopyridine and 2-aminothiazole and removing the acetyl group by hydrolysis.

THE discovery by Domagk (*Klin. Woch.*, 1942, **21**, 448; *Deutsch. med. Wschr.*, 1943, **69**, 379) that marfanil, which is *p*-sulphonamidobenzylamine hydrochloride (Miller, Sprague, Kissinger, and McBurney, *J. Amer. Chem. Soc.*, 1940, **62**, 2099; Klarer, *Klin. Woch.*, 1941, **20**, 1250), possesses considerable activity against

anaerobes both *in vitro* and *in vivo* has resulted in the investigation of a number of related compounds (Evans, Fuller, and Walker, *Lancet*, 1944, **247**, 523). The present communication records the preparation of a number of sulphonamides derived from *p*-sulphobenzylaniline. Access to compounds of this type could be obtained through aceto-*p*-chlorosulphonylbenzylanilide (I), which should be the main product of the chlorosulphonation of acetobenzylanilide. It is stated (Soc. des Usines Chimiques Rhône-Poulenc, B.P. 483,945) that the product of this reaction is N^4-benzylacetylsulphanilyl chloride (II), since by the action of aqueous ammonia it is converted into N^4-benzylsulphanilamide, m. p. 175°, identical with that obtained by benzylating sulphanilamide or by the reduction of N^4-benzylidenesulphanilamide (B.P. 465,914). Repetition of the

chlorosulphonation as described in the patent resulted in a 43% yield of a *sulphonyl chloride*, m. p. 107°, and an oil which on solution in ether and precipitation with light petroleum deposited an isomeric *sulphonyl chloride*, m. p. 80—83°. Amidation of the sulphonyl chloride of lower m. p. afforded *aceto*-m-*sulphonamidobenzylanilide*, m. p. 145°, which was oxidised by alkaline potassium permanganate to *m*-sulphonamidobenzoic acid. The higher-melting sulphonyl chloride does not suffer hydrolysis during amidation as stated in the patent, but yields a sulphonamide, m. p. 177°, which depresses the melting point of N^4-benzylsulphanilamide and must be aceto-*p*-sulphonamidobenzylanilide, since by successive oxidation with alkaline potassium permanganate and esterification it affords ethyl *p*-sulphonamidobenzoate. Amidation of the liquid mixture of sulphonyl chlorides and separation of the resulting isomeric sulphonamides by fractional crystallisation from methyl alcohol indicated that the chlorosulphonation of aceto-*p*-chlorosulphonylbenzylanilide results in the production of aceto-*p*-sulphonamidobenzylanilide and its *m*-isomer in the ratio 4 : 1, but owing to the ease with which the *m*-chloride is hydrolysed the estimate of the proportion of the *m*-isomeride must be regarded as a conservative one. The yield of the two sulphonyl chlorides was approximately 69% and if isomers sulphonated in the aniline nucleus were produced, they must have suffered hydrolysis when the sulphonation mixture was quenched in ice-water. Blangey, Fierz-David, and Stamm (*Helv. Chim. Acta*, 1942, **25**, 1162) have shown that benzylethylaniline undergoes predominant *m*-substitution in the benzyl nucleus with excess of chlorosulphonic acid and we attribute the formation of a smaller proportion of the *m*-isomeride in the chlorosulphonation of acetobenzylanilide to inhibition of salt formation by the acetyl radical.

Condensation of aceto-*p*-chlorosulphonylbenzylanilide with methylamine, guanidine, 2-aminopyridine and 2-aminothiazole respectively, followed by hydrolysis, afforded p-*sulphonmethylamidobenzylaniline* (III), m. p. 92—93°, p-*sulphonguanylamidobenzylaniline* (IV), m. p. 206°, p-*sulphon*-2′-*pyridylamidobenzylaniline* (V), m. p. 206°, and p-*sulphon*-2′-*thiazolylamidobenzylaniline* (VI), m. p. 188—190°.



The activity of these compounds against a number of bacteria has been determined by Mr. C. E. Coulthard, M.P.S., whose results will be reported elsewhere.

Experimental.

Acetochlorosulphonylbenzylanilides.—Acetobenzylanilide (112 c.c.) was slowly added with mechanical stirring, so that the temperature did not exceed 25°, to chlorosulphonic acid (164 c.c.; 5·0 mols.). After being kept overnight, the mixture was maintained at 65° for 2—3 hours, cooled, and poured into ice-water. The sulphonyl chlorides were extracted with benzene, and the washed and dried solution was concentrated, diluted with light petroleum (b. p. 60—80°), and kept at 0° until crystallisation was complete. After washing with light petroleum the solid (69 g.) melted at 85—97° and recrystallisation from light petroleum–benzene afforded *aceto*-p-*chlorosulphonylbenzylanilide*, m. p. 107° (Found : Cl, 11·0. $C_{15}H_{14}O_3NClS$ requires Cl, 11·0%). The liquid portion of the sulphonyl chlorides was dissolved in ether and precipitated with light petroleum, giving first a precipitate (9 g.), m. p. *ca.* 75°, and then a further yield of the *p*-sulphonyl chloride. Recrystallisation from xylene–light petroleum afforded *aceto*-m-*chlorosulphonylbenzylanilide*, m. p. 80—83° (Found : Cl, 11·1%).

Sulphonamidobenzylanilides.—*Aceto*-p-*sulphonamidobenzylanilide*, m. p. 178° (Found : N, 9·0. $C_{15}H_{16}O_3N_2S$ requires N, 9·2%), and *aceto*-m-*sulphonamidobenzylanilide*, m. p. 145° (Found : N, 9·1%), were obtained in 96% yield by shaking the afore-mentioned sulphonyl chlorides (15 g.) with 19% aqueous ammonia (162 c.c.; 36 mols.) for 50 minutes and crystallising the products from alcohol. Admixture of the *p*-isomer with N^4-benzylsulphanilamide, m. p. 178—179° (Found : N, 10·7. $C_{13}H_{14}O_2N_2S$ requires N, 10·7%), prepared by the benzylation of sulphanilamide (B.P. 465,914), depressed the m. p. to 145—155°. Hydrolysis of aceto-*p*-sulphonamidobenzylanilide by heating on the steam-bath for 24 hours with 2·5N-sodium hydroxide (8·0 mols.) afforded a quantitative yield of p-*sulphonamidobenzylaniline*, m. p. 144—145° (Found : C, 60·0; H, 5·6. $C_{13}H_{14}O_2N_2S$ requires C, 59·2; H, 5·3%). Aceto-*p*-sulphonamidobenzylanilide (5 g.) was dissolved in 5N-sodium hydroxide and stirred mechanically during the slow addition of a solution of potassium permanganate (7·5 g., equivalent to 4·3 atoms of oxygen) in water (150 c.c.). After being stirred for 24 hours, the mixture was heated on the steam-bath for an hour and afforded *p*-sulphonamidobenzoic acid (2·6 g.), m. p. 280° (decomp.) (Found : N, 7·3. Calc. for $C_7H_7O_4NS$: N, 7·0%), which was esterified by solution in 10% ethyl-alcoholic hydrogen chloride. The ethyl *p*-sulphonamidobenzoate so obtained has m. p. 112°, undepressed on admixture with an authentic specimen (Remsen, *Annalen*, 1875, **178**, 300). Oxidation of aceto-*m*-sulphonamidobenzylanilide

similarly afforded *m*-sulphonamidobenzoic acid (Found: N, 7·1%), m. p. and mixed m. p. 248—249°, which was converted into its ethyl ester, m. p. and mixed m. p. 129°. *Ethyl* m-*sulphonamidobenzoate*, prepared by refluxing *m*-sulphonamidobenzoic acid (10 g.), ethyl alcohol (25 c.c.), and concentrated sulphuric acid (2 c.c.) for 80 minutes, separated from 50% aqueous alcohol in flat needles, m. p. 129° (Found: N, 6·25. $C_9H_{11}O_4NS$ requires N, 6·1%). Yield, 10·2 g. (89%).

p-*Sulphonmethylamidobenzylaniline*.—When aceto-*p*-chlorosulphonylbenzylanilide (20 g.) was shaken for ½ hr. with excess of 20% aqueous methylamine, *aceto*-p-*sulphonmethylamidobenzylanilide*, m. p. 138—139° (Found: N, 8·8. $C_{16}H_{18}O_3N_2S$ requires N, 8·8%), was obtained in 81·5% yield and hydrolysis by heating on the steam-bath with 2·5N-sodium hydroxide gave p-*sulphonmethylamidobenzylaniline*, m. p. 92—93° (Found: N, 10·35. $C_{14}H_{16}O_2N_2S$ requires N, 10·15%).

p-*Sulphonguanylamidobenzylaniline*.—A solution of aceto-*p*-chlorosulphonylbenzylanilide (32 g.) in acetone (80 c.c.) was added below 10° to an alkaline solution of guanidine prepared from guanidine nitrate (13 g.; 1·1 mols.), sodium hydroxide (10 g.; 2·5 mols.), water (20 c.c.), and acetone (40 c.c.). After being stirred for 2 hours at room temperature, the solution was made alkaline to litmus, and the solvent removed by distillation. The residue was diluted with water, made alkaline to brilliant-yellow and filtered (32 g. or 93%). Recrystallisation from 5N-acetic acid afforded *aceto*-p-*sulphonguanylamidobenzylanilide* as a white powder, m. p. 250—257° (decomp.) (Found: N, 15·9. $C_{16}H_{18}O_3N_4S$ requires N, 16·2%). Hydrolysis was effected by boiling the acetyl derivative (10 g.) with 6N-hydrochloric acid (20 c.c.) for 10 minutes, diluting the solution with water, removing unchanged material, and treating the filtrate with alkali. The recovered material was hydrolysed in the same way and the operations repeated until the whole of the acetyl derivative had been hydrolysed. Recrystallisation from aqueous alcohol afforded 4·3 g. (46%) of a *monohydrate*, m. p. 186—187° (Found: H_2O, 5·5. $C_{14}H_{16}O_2N_4S,H_2O$ requires H_2O, 5·6%), which on drying at 100° gave anhydrous p-*sulphonguanylamidobenzylaniline*, m. p. 206° (Found: C, 55·0; H, 5·3. $C_{14}H_{16}O_2N_4S$ requires C, 55·3; H, 5·3%).

p-*Sulphon-2′-pyridylamidobenzylaniline*.—Aceto-*p*-chlorosulphonylbenzylanilide (15 g.) was added in portions to a solution of 2-aminopyridine (6 g.; 1·4 mols.) in dry pyridine (40 c.c.; 10·7 mols.), and after keeping for 12 hours, the solution was diluted with water (400 c.c.). The solid was collected, washed with N-acetic acid and recrystallised from methyl alcohol. *Aceto*-p-*sulphon-2′-pyridylamidobenzylanilide* separated in white plates, m. p. 184—185° (Found: C, 63·3; H, 5·1; N, 11·0. $C_{20}H_{19}O_3N_3S$ requires C, 63·0; H, 5·0; N, 11·0%). Yield, 13·5 g. or 76·5%. The acetyl derivative (12 g.) was hydrolysed by heating on the steam-bath for 24 hours with 2·5N-sodium hydroxide (125 c.c.) and the solid, which separated after dilution with water and addition of ammonium chloride, was crystallised from aqueous dioxan (charcoal), yielding p-*sulphon-2′-pyridylamidobenzylaniline* (8·1 g.), m. p. 206° (Found: N, 12·3. $C_{18}H_{17}O_3N_3S$ required N, 12·4%).

p-*Sulphon-2′-thiazolylamidobenzylaniline*.—Aceto-*p*-chlorosulphonylbenzylanilide (16 g.), 2-aminothiazole (7 g.; 1·4 mols.), and the minimum quantity of dry pyridine, when kept for 24 hours and poured into water, afforded a buff solid, which, when washed with water and crystallised from alcohol, gave white plates (13 g. or 68%) of *aceto*-p-*sulphon-2′-thiazolylamidobenzylanilide*, m. p. 197—198° (Found: N, 10·95. $C_{18}H_{17}O_3N_3S_2$ requires N, 10·85%). The acetyl derivative (14·8 g.) was hydrolysed by heating with 2·5N-sodium hydroxide for 24 hours at 100° and precipitating with ammonium chloride. The product (13·8 g.) was recrystallised from aqueous dioxan, giving colourless needles (9·75 g. or 74%) of p-*sulphon-2′-thiazolylamidobenzylaniline*, m. p. 188—190° (Found: C, 55·5; H, 4·35. $C_{16}H_{15}O_3N_3S_2$ requires C, 55·7; H, 4·35%).

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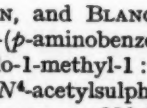
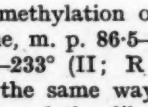
65. *Alkyl Derivatives of Sulphapyridine.*

By W. KELLY and W. F. SHORT.

In agreement with Shepherd, Bratton, and Blanchard (*J. Amer. Chem. Soc.*, 1942, **64**, 2532) methylation of sulphapyridine or its N^4-acetyl derivative with methyl sulphate and alkali produces derivatives of 1-methyl-1 : 2-dihydropyridine as main product. Benzylation of sulphapyridine, however, produces either N^4-benzylsulphapyridine or 2-sulphanilimido-1-benzyl-1 : 2-dihydropyridine according to the experimental conditions employed.

SHEPHERD, BRATTON, and BLANCHARD (*loc. cit.*) showed that methylation of sulphapyridine with diazomethane afforded 2-(*p*-aminobenzenesulphonmethylamido)pyridine, m. p. 86·5—87·5° (I; R = Me, R′ = H) and 2-sulphanilimido-1-methyl-1 : 2-dihydropyridine, m. p. 232—233° (II; R = Me, R′ = H), in the ratio 70 : 30, and when N^4-acetylsulphapyridine was methylated in the same way, the product contained the N^1-methyl derivative, m. p. 119·5—120° (I ; R = Me, R′ = Ac) and the dihydropyridine derivative, m. p.

(I.)  (II.) 

239—240° (II; R = Me, R′ = Ac) in the ratio 60 : 40. Methylation of sulphapyridine and its N^4-acetyl derivative with methyl sulphate in aqueous solution was shown to yield 2-sulphanilimido-1-methyl-1 : 2-dihydropyridine (II; R = Me, R′ = H) and the corresponding N^4-acetyl derivative (II; R = Me, R′ = Ac) respectively, the yield being 40—50% in each case.

The experiments here described were completed in September, 1942, and since our conclusions are in substantial agreement with those of the American authors it is unnecessary to repeat the experimental details in cases where duplication has occurred. It is stated in B.P. 512,145 that a methyl group is introduced into the sulphimido-group when sulphapyridine or its N^4-acetyl derivative is methylated with methyl sulphate and alkali, the products melting at 225° and 231° respectively, and the acetyl compound also being obtained from 2-bromopyridine and *p*-acetamidobenzenesulphonamide. Repetition of the methylations as described

in the patent afforded 2-sulphanilimido-1-methyl-1 : 2-dihydropyridine, m. p. 232—233°, in 57% yield and its constitution was established both by synthesis from and by degradation to 1-methyl-1 : 2-dihydropyridine. Methylation of N^4-acetylsulphapyridine with the same reagents afforded the corresponding acetyl derivative (II; R = Me, R′ = Ac), m. p. 239—240°, in 93% yield and hydrolysis of the crude methylation product, m. p. 226—228°, afforded 2-methylaminopyridine in an amount which indicated the presence of 2—3% of the isomeric N^4-acetyl-N^1-methylsulphanilamidopyridine (I; R = Me, R′ = Ac). Under these conditions methylation therefore occurs to some extent in the sulphamido-group, as suspected by the American authors. When 2-methylaminopyridine and *p*-acetamidobenzenesulphonyl chloride were condensed under the conditions prescribed in B.P. 512,145, 2-sulphanilamido-N^4-acetyl-N^1-methylpyridine (I; R = Me; R′ = Ac), m. p. 117·4—118·4° (free amine, m. p. 87—88°), was obtained in 71% yield.

We find that benzylation of sulphapyridine results in the attachment of a benzyl group either at N^4 or at the pyridine nitrogen according to the experimental conditions employed. Thus, benzylation of sulphapyridine with benzyl chloride in alkaline *aqueous* solution is reported in B.P. 512,145 to yield 2-sulphanilamido-N^1-benzylpyridine (I; R = CH_2Ph, R′ = H), m. p. 179°. Repetition of the experiment, however, gave a 38% yield of a compound, m. p. 186°, which must be N^4-*benzylsulphapyridine* (I; R = H, R′ = CH_2Ph), since on hydrolysis it yields *benzylsulphanilic acid* and may also be obtained by condensing 2-bromopyridine with N^4-benzylsulphanilamide. Benzylation of sulphapyridine or N^4-acetylsulphapyridine in alkaline *aqueous-alcoholic* solution affords 2-sulphanilimido-1-benzyl-1 : 2-dihydropyridine (II; R = CH_2Ph, R′ = H), m. p. 239—240°, and its acetyl derivative (II; R = CH_2Ph, R′ = Ac), m. p. 213—214°, respectively. These compounds were prepared in the same way by Shepherd *et al.* (*loc. cit.*), who record m. p. 235° and 213—214° respectively. In agreement with them we find that the acetyl derivative prepared from 2-imino-1-benzyl-1 : 2-dihydropyridine and *p*-acetamidobenzenesulphonyl chloride melts at 213—214° and not at 188—190° as recorded by Polyakova and Kirsanov (*J. Appl. Chem. Russia*, 1940, **13**, 1215).* Finally, by condensing 2-benzylaminopyridine with *p*-acetamidobenzenesulphonyl chloride, we obtained 2-*sulphanilamido*-N^4-*acetyl*-N^1-*benzylpyridine* (I; R = CH_2Ph, R′ = Ac), m. p. 186—187°, and this compound afforded 2-*sulphanilamido*-N^1-*benzylpyridine*, m. p. 134—135°, on hydrolysis.

Experimental.

N^4-*Benzylsulphapyridine.*—Benzyl chloride (40 c.c., 7 mols.) was added slowly with mechanical stirring to a solution of sulphapyridine (12·5 g.) in 2N-sodium hydroxide (30 c.c., 1·2 mols.) and water (40 c.c.), the mixture stirred for an hour, ether (100 c.c.) added, and the solid washed with dilute hydrochloric acid and recrystallised from alcohol. The crude solid (6·5 g. or 38%), m. p. 179—180°, on further recrystallisation from alcohol afforded N^4-*benzylsulphapyridine* in colourless plates, m. p. 186° (Found: C, 64·0; H, 5·2; N, 12·4. $C_{18}H_{17}O_2N_3S$ requires C, 63·7; H, 5·1; N, 12·5%). N^4-Benzylsulphanilamide (5·2 g.; Kelly, Robson, and Short, preceding paper), 2-bromopyridine (3·2 g.), potassium carbonate (2·8 g.), and copper powder (0·2 g.) gave the same compound in 21% yield when maintained at 200° for an hour. Hydrolysis of this compound (6 g.) by boiling for 4 hours with 36% hydrochloric acid (20 c.c.) gave *benzylsulphanilic acid* (3·7 g.), which was dried at 120° (Found: C, 58·8; H, 5·4; N, 5·0; *M*, by titration, 259. $C_{13}H_{13}O_4NS$ requires C, 59·3; H, 5·0; N, 5·3%; *M*, 263). This acid, which did not melt below 270°, was identical in properties with a specimen prepared from sulphanilic acid and benzyl chloride in aqueous alkaline solution.

2-*Sulphanilimido*-1-*benzyl*-1 : 2-*dihydropyridine.*—2-Imino-1-benzyl-1 : 2-dihydropyridine (3·7 g.), prepared as described by Tschitschibabin, Konowalowa, and Konowalowa (*Ber.*, 1921, **54**, 821), and *p*-acetamidobenzenesulphonyl chloride (2·4 g.; 0·5 mol.) afforded 2-sulphanilimido-N^4-acetyl-1-benzyl-1 : 2-dihydropyridine, which separated from alcohol in large colourless prisms, m. p. 213—214° (Found: C, 62·8; H, 5·2; N, 11·0. Calc. for $C_{20}H_{19}O_3N_3S$: C, 63·0; H, 5·0; N, 11·0%). The yield was 48·5% and a considerably lower yield (10%) was obtained when the condensation was effected in presence of pyridine. Addition of benzyl chloride (10 c.c.; 1·7 mols.) to a solution of sulphapyridine (15 g.) in 5N-sodium hydroxide (20 c.c.; 1·9 mols.) and alcohol (60 c.c.), followed by heating at 80° for 10 minutes and keeping for 16 hours, produced the same compound, m. p. and mixed m. p. 213—214°, in 53% yield. Hydrolysis of the acetyl derivative was effected by heating with alcohol and concentrated hydrochloric acid and crystallisation from alcohol gave 2-sulphanilimido-1-benzyl-1 : 2-dihydropyridine, m. p. 239—240° (Found: C, 63·9; H, 5·2; N, 12·5. Calc. for $C_{18}H_{17}O_2N_3S$: C, 63·7; H, 5·1; N, 12·4%). This compound was also obtained in 18% yield from sulphapyridine (15 g.), benzyl chloride (10 c.c., 1·5 mols.), 5N-sodium hydroxide (30 c.c., 2·5 mols.), and alcohol (70 c.c.) by heating on the steam-bath for 5 minutes.

2-*Sulphanilamido*-N^1-*benzylpyridine.*—*p*-Acetamidobenzenesulphonyl chloride (4·75 g.) was added to a solution of 2-benzylaminopyridine (3·7 g.), prepared as described by Tschitschibabin *et al.* (*loc. cit.*, p. 822), in dry pyridine (10 c.c.), and the mixture heated on the steam-bath for 15 minutes. The solid which separated on dilution of the cold reaction product with water (30 c.c.) was recrystallised from methyl alcohol, giving cubes or slender felted needles (3 g. or 39%) of 2-*sulphanilamido*-N^4-*acetyl*-N^1-*benzylpyridine*, m. p. 186—187° (Found: C, 62·7; H, 5·0; N, 11·1. $C_{20}H_{19}O_3N_3S$ requires C, 63·0; H, 5·0; N, 11·0%). Hydrolysis of the acetyl derivative (1 g.) was effected by boiling for an hour with alcohol (50 c.c.) and 5N-sodium hydroxide (5 c.c.). Crystallisation of the product from alcohol gave 2-*sulphanilamido*-N^1-*benzylpyridine*, m. p. 134—135° (Found: C, 63·6; H, 5·2; N, 12·3. $C_{18}H_{17}O_2N_3S$ requires C, 63·7; H, 5·1; N, 12·4%).

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* Only an abstract of this paper was available and the discrepancy may be due to a typographical error.

66. *The Behaviour of Keten towards Olefins and Olefinic Peroxides.*

By Ralph F. Naylor.

Keten will not react additively with unconjugated olefins such as 1-methyl*cyclo*hexene, dihydromyrcene, and rubber. Zinc chloride or sulphuric acid promotes reaction of keten with acetone (carried over from the keten generator), with the formation of a compound $C_7H_{10}O_3$, probably β-propenyl acetoacetate. Keten acetylates olefinic hydroperoxides, but the resultant peracetates are very unstable.

Several groups of workers have shown that diphenylketen will add to both conjugated and unconjugated olefins, including *cyclo*pentadiene, *cyclo*hexene, *cyclo*hexadiene, 2 : 3-dimethylbutadiene and $\Delta^{\alpha\gamma}$-pentadiene, with formation of *cyclo*butanone derivatives. The only recorded work, however, on the addition of keten to olefins is that of Brooks and Wilbert (*J. Amer. Chem. Soc.*, 1941, **63**, 870), who showed that it reacts under pressure at 100° with an equimolecular quantity of *cyclo*pentadiene to give the *bicyclo*[0 : 2 : 3]heptenone. An attempt has now been made to add keten to representative mono-olefins and unconjugated di- and poly-olefins, in the examples of 1-methyl*cyclo*hexene, dihydromyrcene and rubber, at temperatures ranging from 20° to 120°, either under pressure with the olefins alone, or with solutions of the olefins in suitable solvents (chloroform, toluene, and ether). Under these conditions, no action occurred except the formation of diketen; when, however, sulphuric acid or, better, zinc chloride was added as a catalyst, a small quantity of a high-boiling liquid was formed, even when the olefin was omitted from the reaction mixture. This liquid was a *compound* $C_7H_{10}O_3$, derived apparently by reaction of keten with small quantities of acetone which had been carried over from the keten generator. Keten reacts with acetone in presence of sulphuric acid to give the acetate (I) derived from the enolic form of the ketone (Gwynn and Degering, *J. Amer. Chem. Soc.*, 1942, **64**, 2216):

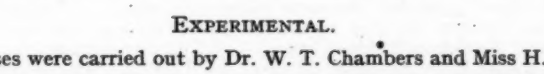
$$CH_2{:}CO + HO{\cdot}CMe{:}CH_2 \longrightarrow CH_3{\cdot}CO{\cdot}O{\cdot}CMe{:}CH_2 \quad (I.)$$

Other products obtained by these authors were diketen and a higher-boiling residue which they did not identify. It was probably the compound $C_7H_{10}O_3$ now isolated. Hurd and Williams (*ibid.*, 1936, **58**, 964) have shown that the dimer of keten can behave as acetylketen and it seems probable that this substance has in the present instance reacted with enolic acetone in the same way as does keten, with the formation of β-propenyl acetoacetate (II):

$$CH_3{\cdot}CO{\cdot}CH{:}CO + HO{\cdot}CMe{:}CH_2 \longrightarrow CH_3{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}O{\cdot}CMe{:}CH_2 \quad (II.)$$

Although insufficient ester was separated for complete identification, the above formula is supported by all the available evidence (see experimental part).

To test the possibility that olefinic hydroperoxides might be stabilised by acetylation with keten, the reaction between keten and Δ^2-*cyclo*hexene hydroperoxide was examined. It proceeded readily at room temperature, but the product was almost entirely Δ^2-*cyclo*hexenyl acetate. At a lower temperature the acetate was accompanied by some peracetate, which would consequently appear to be the primary product of reaction:



Rubber was not greatly attacked by keten, but when it was treated concurrently with oxygen and keten it broke down oxidatively much more rapidly than when treated with oxygen alone, the percentage of oxygen absorbed after 12 hours being 1·7 and 0·2 respectively. This also would seem to indicate the greater instability of the peracetate groups.

Experimental.

(Microanalyses were carried out by Dr. W. T. Chambers and Miss H. Rhodes.)

Interaction of Keten and Acetone.—Keten (15 g.) as obtained from the generator (Williams and Hurd, *J. Org. Chem.*, 1940, **5**, 122) contained a little acetone; it was passed into dry ether (30 ml.) at − 60°. After addition of zinc chloride (0·3 g.) as catalyst, the solution was heated in a sealed tube for 4 hours at 100°. The bulk of the ether and unchanged keten were then removed, benzene (40 ml.) added, and the zinc chloride extracted with water. After removal of solvent, fractionation of the product gave diketen and a liquid (*ca.* 1 g.), b. p. 40°/0·03 mm., $n_D^{18°}$ 1·4632 (Found: C, 59·1; H, 7·2. $C_7H_{10}O_3$ requires C, 59·15; H, 7·0%).

The product dissolved to a slight extent in water, so forming a faintly acid solution which gave a red colour with ferric chloride, and in aqueous alcohol it rapidly reduced alkaline potassium permanganate. The iodine value (Kemp, Bishop, and Lasselle, *Ind. Eng. Chem.*, 1931, **33**, 1445) was 38 after 1 hour and *ca.* 190 after eighteen hours ($C_7H_{10}O_3$ requires I.V. 89·4). Attempted preparation of the oxime gave only an oil, and condensation with dinitrophenylhydrazine in alcoholic sulphuric acid solution gave acetonedinitrophenylhydrazone, the acid conditions of reaction leading to hydrolysis of the ester; this observation corresponds exactly to that of Gwynn and Degering (*loc. cit.*) with the β-propenyl acetate obtained from keten and acetone. The derivative, after chromatography in benzene solution through alumina, crystallised from 95% alcohol in orange plates, m. p. 125°. The dinitrophenylhydrazone prepared from pure acetone and a mixture of the two also melted at 125° (Found: C, 45·5; H, 4·3; N, 23·6. Calc. for $C_9H_{10}O_4N_4$: C, 45·4; H, 4·2; N, 23·5%).

Absorption spectra: In water, a band ($\varepsilon = 8500$) at λ 255. In *cyclo*hexane, a band ($\varepsilon = 10{,}000$) at λ 240. The absorption in aqueous solution was unchanged by addition of acid or alkali.

Interaction of Keten and Δ^2-cyclo*Hexene Hydroperoxide.*—To the hydroperoxide (3·7 g.) (Farmer and Sundralingam, J., 1942, 132) in toluene (5 ml.) at − 70° was added a solution of keten (2 g.) in toluene (30 ml.) at the same temperature. The mixture was allowed to warm slowly, and the temperature eventually rose to 45°. After removal of the residual keten and toluene, the product (2 g.) was distilled at 27—30°/0·003 mm. This liquid contained only 0·75%

of peroxide and consisted almost entirely of an acetic *ester*, probably Δ^1-*cyclo*hexenyl acetate (Found: C, 67·8; H, 8·55. $C_8H_{12}O_2$ requires C, 68·6; H, 8·6%).

In an attempt to obtain the undecomposed peracetate the experiment was repeated under carefully controlled conditions. Keten was bubbled through a solution of the peroxide (3 g.) in toluene (40 ml.) at − 70° for 30 minutes. The solution was then allowed to warm very slowly to 0°, and the reaction mixture was worked up as before. A peroxide determination at this stage showed that only a third of the original peroxide oxygen remained. The product consisted mainly of the acetate, b. p. 33—34°/0·05 mm., but a few drops of a liquid, b. p. 55—57°/0·05 mm., were obtained. This strongly peroxidic material was not pure, but its instability and analysis indicated that it was mainly Δ^1-*cyclo*hexenyl peracetate (Found: C, 62·4; H, 8·1. $C_8H_{12}O_3$ requires C, 61·5; H, 7·7%).

Keten and Rubber.—(i) Excess of keten was condensed on sol rubber * (1 g.) at −100° in absence of air, and the mixture allowed to warm very slowly to 20°. Swelling of the rubber occurred. Some diketen was formed and was removed under reduced pressure; the product was then washed with acetone and dried in a high vacuum [Found: C, 86·6; H, 11·65; O (diff.), 1·75. Found for the original rubber: C, 87·55; H, 11·8; O (diff.), 0·65%]. Although only 1·1% of oxygen had entered the molecule, the rubber had become insoluble in benzene.

(ii) Oxygen was passed through a 1% solution of sol rubber in methyl*cyclo*hexane for 2 hours, and this was followed by the passage for 10 hours of oxygen and keten. Keten, diketen, and the solvent were removed under reduced pressure, and the rubber was dissolved in benzene before precipitation by alcohol [Found: C, 85·9; H, 11·75; O (diff.), 2·35; *M* (viscosity), 31,000. Found for the original rubber: C, 87·55; H, 11·8; O (diff.), 0·65%; *M* (viscosity), 230,000]. Under similar conditions, but with the omission of keten, a product was obtained [Found: C, 87·35; H, 11·75; O (diff.), 0·9. Found for the original rubber: C, 87·4; H, 11·9; O (diff.), 0·7%].

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67. Delphinium *Alkaloids. Part IV. The Alkaloids of the Seeds of* Delphinium ajacis.

By John A. Goodson.

From the alkaloids of the seeds of *Delphinium ajacis* five crystalline alkaloids amounting to approximately 20% of the total alkaloids of the seeds have been isolated, *viz.*, ajacine, ajaconine, and bases for the present designated "base B," "base C," and "base D."

As in the case of the total alkaloids of the seeds of *Delphinium staphisagria* (Jacobs and Craig, *J. Biol. Chem.*, 1939, **127**, 361), so in that of the total alkaloids of the seeds of *Delphinium ajacis*, only a portion has been obtained in crystalline form. From the seeds of *D. ajacis*, Keller and Völker (*Arch. Pharm.*, 1913, **251**, 209) isolated two crystalline alkaloids, which they named ajacine and ajaconine. Recently, Hunter (*Pharm. J.*, 1943, **150**, 82, 95) briefly reported the isolation of four crystalline alkaloids, *viz.*, ajacine, $C_{32}H_{44}O_8N_2,2H_2O$, ajaconine, $C_{21}H_{31}O_3N$, a new alkaloid ajacinine, $C_{22}H_{37}O_6N$, and an unnamed base, but gave no details of their properties or analyses.

In the present investigation five crystalline alkaloids have been isolated, including ajacine and ajaconine, the others being for the present called "*base B*," "*base C*," and "*base D*," as one of them, possibly "base C," may prove to be identical with Hunter's ajacinine.† Ajacine has been shown to be acetylanthranoyllycoctonine, $C_{34}H_{46}O_9N_2,2H_2O$ (Goodson, J., 1944, 108). It was then assumed that the alkyl group attached to nitrogen was a methyl group, but as shown by Rabinovich and Konovalova [*J. Gen. Chem. U.S.S.R.*, 1942, **12**, 231 (English Summary 328)], in the cases of delphamine from species of *Delphinium* and condelphine from *Delphinium confusum*, var. Pop., the alkyl group of ajacine is now found to be an ethyl group. "Base B," $C_{26}H_{39}O_8N$, and "base C," $C_{24}H_{37}O_7N$, also contain an ethylimino-group, both contain three methoxy-groups, and "base B" on hydrolysis gives "base C" and acetic acid. "Base C" may be a demethyllycoctonine, in which case the relationship of the three alkaloids may be expressed by the following formulæ:

Lycoctonine	$C_{19}H_{19}NEt(OMe)_4(OH)_3$	"Alkaloid B"	$C_{19}H_{19}NEt(OMe)_3(OH)_3{\cdot}OAc$
Ajacine	$C_{19}H_{19}NEt(OMe)_4(OH)_2(O{\cdot}CO{\cdot}C_6H_4{\cdot}NHAc)$	"Alkaloid C"	$C_{19}H_{19}NEt(OMe)_3(OH)_4$

Attempts, however, to prove lycoctonine to be a methyl derivative of "base C" by their conversion into the same hydroxy-compound by demethylation or into the same heptamethoxy-compound by complete methylation were unsuccessful.

Potentiometric titration of ajaconine, which is an *N*-methyl base, gave an equivalent of 362, which is in better accord with the formula $C_{22}H_{33}O_3N$ than with Hunter's formula $C_{21}H_{31}O_3N$. It may be that the formula should be doubled, as the figure obtained for methylimino is only half that required for one methylimino-group in a compound of the formula $C_{22}H_{33}O_3N$. The formula of the *hydriodide* of "base D" is provisionally given as $C_{43}H_{66}O_{12}N_2,HI$; the free base appears to be formed from it by the loss of the elements of a molecule of water in addition to one of hydrogen iodide.

* Obtained by diffusion of acetone-extracted crepe rubber into light petroleum.

† Since the submission of this paper for publication a contribution on the same subject has been made by Hunter (*Quart. J. Pharm.*, 1944, **17**, 302) in which it is seen that the properties of his ajacinine differ somewhat from those of "base C" described above. Direct comparison of a specimen of ajacinine kindly supplied by Dr. Matthew V. Hunter proves it not to be identical with "base C."

Experimental.

The m. p.'s are corrected.

Total Alkaloids.—By the method described below, 31·8 g. of total alkaloids (1·06%) were obtained from 3 kg. of seeds of horticultural origin.

Isolation of Alkaloids.—The crushed seeds (39 kg.) were percolated with 90% alcohol (260 l.). The percolate, concentrated until most of the alcohol had been removed, separated into two layers. The oily layer was extracted three times with 10% hydrochloric acid, and the acid solution added to the main aqueous layer. The united solutions were treated with excess of sodium bicarbonate and extracted twice with an equal volume of chloroform to give the weak bases. The aqueous solution was treated with 25% sodium hydroxide solution and extracted twice with an equal volume of chloroform, yielding the strong bases. The chloroform solutions were shaken with sufficient N-hydrochloric acid to render the mixtures slightly acid to Congo-red paper. In the case of the chloroform solution of the weak bases, both the aqueous layer (A) and the chloroform layer (B) contained hydrochlorides of bases. In the case of the chloroform solution of the strong bases, the hydrochlorides of the bases passed almost completely into the aqueous layer (C). The aqueous layer (A), containing 103 g. of alkaloids (or 0·264% of the seeds), was treated with excess of sodium bicarbonate and extracted six times with an equal volume of ether. The concentrated ethereal solution on long standing deposited 15·1 g. of crystals of crude "base B" (0·0387% of the seeds). The aqueous liquor was extracted three times with an equal volume of chloroform and the alkaloids thus removed were fractionated by shaking the chloroform solution with small quantities of N-hydrochloric acid. The bases, regenerated from the fractions of the hydrochloride, having rotations between $[\alpha]_D$ + 42° and + 50°, on crystallisation from alcohol gave 5·11 g. of crude crystalline "base C" (0·0131% of the seeds).

The chloroform layer (B) was evaporated to dryness, and the residue treated with very dilute hydrochloric acid. The aqueous solution, after separation from tar and purification with charcoal, contained 164 g. of alkaloids (0·421% of the seeds). It was rendered alkaline with sodium bicarbonate and extracted with ether. The ethereal solution on concentration deposited 40·5 g. of crude crystalline ajacine (0·1038% of the seeds) and on further concentration gave 5·8 g. of crude, crystalline "base B" (0·0148% of the seeds). The bases from the mother-liquor were dissolved in alcohol and neutralised with N-hydriodic acid. On keeping in the ice-chest, 7·77 g. (0·0199% of the seeds) of crude crystalline hydriodide of "base D" separated.

"*Base B.*"—The *base*, purified by recrystallisation from alcohol, gave anhydrous crystals, m. p. 195° (sinters at 193°), $[\alpha]_D^{17°}$ + 34·0° (*c* = 1 in dry alcohol), $[\alpha]_D^{17°}$ + 0·5 (*c* = 2 in N/5-hydrochloric acid) (Found: C, 63·1; H, 8·4; N, 3·2; OMe, 18·3; NEt, 7·7; Ac, 7·2; equiv., by potentiometric titration, 493. $C_{26}H_{39}O_8N$ requires C, 63·3; H, 8·0; N, 2·8; 3OMe, 18·9; NEt, 8·7; Ac, 8·7%; equiv., 493). The aurichloride crystallised from alcohol in light yellow, six-sided plates of the *trihydrate*, m. p. 205° (decomp., sinters at 203°) (Found: loss at 105° in a vacuum, 6·3. $C_{26}H_{39}O_8N,HAuCl_4,3H_2O$ requires $3H_2O$, 6·2%). The anhydrous *aurichloride* melted at 205° (decomp., sinters at 203°) (Found: C, 38·1; H, 5·3; N, 1·8; Au, 24·2. $C_{26}H_{39}O_8N,HAuCl_4$ requires C, 38·2; H, 4·9; N, 1·7; Au, 24·1%).

Hydrolysis of "base B." The base (1·17 g.) was dissolved in alcohol (10 c.c.) and heated on the water-bath with 2·7 c.c. of N-sodium hydroxide until most of the alcohol had evaporated. The residue was treated with 10 c.c. of water, and after standing overnight and being scratched, 0·675 g. of basic hydrolytic product ("base C") crystallised in prisms, a further 0·365 g. being obtained by extracting the mother-liquor with chloroform. Acetic acid was shown to be the acid hydrolytic product by the preparation and analysis of the silver salt. The basic product had m. p. 205° (not depressed by "base C"), $[\alpha]_D^{15°}$ + 56·0° (*c* = 1 in dry alcohol), $[\alpha]_D^{15°}$ + 36·3° (*c* = 2 in N/5-hydrochloric acid) (Found: C, 63·8; H, 8·5; N, 3·4; OMe, 22·3; NEt, 8·8; equiv., by potentiometric titration, 451. Calc. for "base C," $C_{24}H_{37}O_7N$: C, 63·8; H, 8·3; N, 3·1; 3OMe, 20·6; NEt, 9·5%; equiv., 451).

"*Base C.*"—The base, purified by recrystallisation from alcohol, formed anhydrous prisms, m. p. 206° (sinters at 200), $[\alpha]_D^{15°}$ + 57·0° (*c* = 1 in dry alcohol), $[\alpha]_D^{15°}$ + 36·4° (*c* = 2 in N/5-hydrochloric acid) (Found: C, 63·8; H, 8·6; N, 3·5; OMe, 19·5; NEt, 8·2%; equiv., by potentiometric titration, 451). The aurichloride crystallised from dilute alcohol as a *monohydrate* in plates, m. p. 169° (decomp., sinters at 165°) (Found: loss at 105° in a vacuum, 1·6. $C_{24}H_{37}O_7N,HAuCl_4,H_2O$ requires H_2O, 2·2%); the anhydrous *salt* melted at 171° (Found: C, 36·6; H, 5·2; Au, 25·0. $C_{24}H_{37}O_7N,HAuCl_4$ requires C, 36·6; H, 4·8; Au, 24·9%).

Hydriodide of "Base D."—The *hydriodide*, recrystallised from 70% alcohol, gave needles, m. p. 213° (sinters at 207°), $[\alpha]_D^{15°}$ + 32·4° (*c* = 2 in N/5-alcoholic potassium hydroxide) (Found, in air-dried substance: loss at 105° in a vacuum, 3·5. $C_{48}H_{66}O_{12}N_2,HI,2H_2O$ requires $2H_2O$, 3·5%. Found, in *anhydrous* salt: C, 58·1; H, 6·8; N, 3·0; I, 12·8; OMe, 9·4; NMe, 3·3 or NEt, 4·9. $C_{48}H_{66}O_{12}N_2,HI$ requires C, 58·2; H, 6·8; N, 2·8; I, 12·8; 3OMe, 9·4; NMe, 2·9 or NEt, 4·3%).

"*Base D.*"—The free *base*, liberated from the hydriodide by sodium bicarbonate solution and extracted with chloroform, gave anhydrous crystals from 70% alcohol, m. p. 97° (sinters at 80°), $[\alpha]_D^{18°}$ + 59·3° (*c* = 2 in dry alcohol) (Found: C, 68·3; H, 7·5; N, 3·5; OMe, 11·3; NMe, 3·3 or NEt, 4·9. $C_{48}H_{64}O_{11}N_2$ requires C, 68·2; H, 7·6; N, 3·3; 3OMe, 11·0; NMe, 3·4 or NEt, 5·0%).

Ajaconine Sulphate.—The sulphate, purified by recrystallisation from dilute acetone, gave six-sided plates of the *heptahydrate*, m. p. 113° (sinters at 110°), $[\alpha]_D^{23°}$ + 5·5° (*c* = 2 in water) [Found: loss at 70—105° in a vacuum, 12·9. $(C_{22}H_{33}O_3N)_2,H_2SO_4,7H_2O$ requires $7H_2O$, 13·4%]. The anhydrous *sulphate* melted at 231° (decomp., sinters at 214°) (Found: S, 3·9; OMe, nil; NMe, 3·6. $(C_{22}H_{33}O_3N)_2,H_2SO_4$ requires S, 3·9; 2NMe, 7·1%].

Ajaconine.—The base, liberated from the solution of the sulphate by sodium hydroxide solution and extracted by chloroform, crystallised from dilute alcohol in anhydrous prisms, m. p. 172° (sinters at 170°), $[\alpha]_D^{18°}$ − 119·0° (*c* = 2 in dry alcohol) (Found: C, 73·5; H, 9·2; N, 4·2; OMe, nil; NMe, 3·6; equiv., by titration with N/10-sulphuric acid and methyl-red as indicator, 361·5; equiv., by potentiometric titration, 362. Calc. for $C_{22}H_{33}O_3N$: C, 73·5; H, 9·3; N, 3·9; NMe, 8·1%; equiv., 359).

Hydrogenation of ajaconine. Ajaconine (0·5 g.), dissolvd in acetic acid (20 c.c.) and hydrogenated in presence of palladium-black, took up 28·5 c.c. of hydrogen at 17°/763 mm. ($C_{22}H_{33}O_3N$ for 2H requires 33 c.c.). Lycoctonine and "base C" evolve ethyl iodide (identified by conversion into trimethylethylammonium iodide) in Herzig and Meyer's process for the estimation of methylimino-groups, showing them to be ethylimino-compounds. Ajaconine in like circumstances gives methyl iodide (identified by conversion into tetramethylammonium iodide) and is therefore a methylimino-compound.

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NOTES.

Reactivity of Isoprenic and Analogous Hydrocarbons towards Thiocyanic Acid and Dithiocyanogen.

By RALPH F. NAYLOR.

BY analogy with hydrogen halides and hydrogen sulphide (Duffey, Snow, and Keyes, *Ind. Eng. Chem.*, 1934, **26**, 91; Ipatieff and Friedman, *J. Amer. Chem. Soc.*, 1939, **61**, 71; Vaughan and Rust, *J. Org. Chem.*, 1942, **7**, 472) it is reasonable to expect thiocyanic acid to react with olefins, and it has been reported by Kharasch, May, and Mayo (*J. Amer. Chem. Soc.*, 1937, **59**, 1580) that it will add to *iso*butylene at room temperature to give a mixture of *tert.*-butyl thiocyanate and *iso*thiocyanate. Under similar conditions in the present work, the only product that was obtained from *cyclo*hexene and thiocyanic acid was a small quantity of an amorphous powder, probably mainly a perthiocyanic acid, formed by elimination of hydrogen cyanide from three molecules of thiocyanic acid. This tendency towards decomposition of the reagent prevented the use of elevated temperatures, and when methyl thiocyanate (a potential source of SCN and Me radicals by thermal decomposition) was heated at 170° with 1-methyl*cyclo*hexene and a little benzoyl peroxide (as catalyst), it underwent but slight reaction, the drop or two of product giving analytical values which suggested that it might be an impure adduct. Attempts to catalyse the addition of thiocyanic acid to rubber included the use of ultra-violet irradiation, and of aluminium chloride or ferric chloride as catalyst. The most successful of these attempts was with ultra-violet light, but even then the product contained only 1·95% of sulphur, which represented 6% addition to the double bonds of rubber.

Although dithiocyanogen is known to add readily to many unsaturated compounds (Kaufmann, *Ber. deut. pharm. Ges.*, 1923, **33**, 139; Kaufmann and Liepe, *Ber.*, 1923, **56**, 2514), the only reference to its reaction with *cyclo*hexene indicated that addition was very slow, and no product was isolated (Oda, Tamura, and Imai, *Sci. Papers Inst. Phys. Chem. Research, Tokyo*, 1938, **34**, 610). It has now been established that 1-methyl*cyclo*hexene reacts very readily with nascent dithiocyanogen in chloroform. With rubber the reaction proceeds readily with pre-prepared dithiocyanogen, as has been observed by several workers, and by varying the quantities used products were prepared in which 7—100% of the unsaturation was destroyed. In every case gelling started after about 1 hour, increased concurrently with addition of dithiocyanogen, and was not complete for several hours. With nascent dithiocyanogen, however, reaction was complete within a few minutes.

Addition of Thiocyanic Acid to Rubber.—A 10% ethereal solution of thiocyanic acid was prepared from sodium thiocyanate by the method of Klason (*J. pr. Chem.*, 1887, **35**, 407). Treatment of a 10% carbon tetrachloride solution of milled crepe with this solution in daylight at 15° gave products containing, after 24 hours 0·07% of sulphur, and after 120 hours 0·245%. A similar experiment in *cyclo*hexane solution at 0° in the dark gave values of 0·32% and 0·25% respectively.

When a mixture of a 10% carbon tetrachloride solution of milled crepe (50 ml.) and 10% ethereal thiocyanic acid (100 ml.) contained in a quartz flask was irradiated with ultra-violet light for 1½ hours, only 0·05% of sulphur entered the rubber. The experiment was repeated, acetone being added as a photosensitiser and the mixture sealed under nitrogen (at 360 mm.) in a Pyrex tube. After 16 hours' irradiation at 25—30° the product contained 1·95% of sulphur.

With ferric chloride and aluminium chloride as catalyst after 3 days in daylight at 15° products were obtained containing 0·6% and 0·85% of sulphur respectively.

Addition of Dithiocyanogen to 1-*Methyl*cyclo*hexene.*—Lead thiocyanate (40 g.) was stirred as a suspension in chloroform (120 ml.) and methyl*cyclo*hexene (10 g.) at 0°, and phenyl iodochloride (29 g.) added in small quantities. The mixture was stirred at 0° for 5 hours and then kept overnight at that temperature. The lead chloride was filtered off, and excess of dithiocyanogen destroyed by shaking the solution with sodium thiosulphate solution (40 g. in 120 ml. of water). From the dried solution, chloroform was removed by distillation at atmospheric pressure, and iodobenzene and unchanged methyl*cyclo*hexene similarly at 13 mm. pressure. 1 : 2-*Dithiocyano*-1-*methyl*cyclo*hexane* distilled at 100—106°/0·1 mm. as a heavy, viscous, yellow oil, which solidified on cooling to 0° (Found: C, 50·8; H, 5·9; N, 12·9; S, 30·4. $C_9H_{12}N_2S_2$ requires C, 50·9; H, 5·7; N, 13·2; S, 30·2%).

Addition of Dithiocyanogen to Rubber.—Dithiocyanogen was prepared by reaction of lead thiocyanate (8 g.) with bromine (3·2 g.) in carbon tetrachloride or disulphide (100 ml.) at 0°. To 25 ml. of this solution were added 100 ml. of a 1% carbon disulphide solution of milled acetone-extracted crepe. After 40 minutes some of the product was separated by precipitation with alcohol (Found: S, 1·6%), and the remainder, which started gelling after about 1½ hours, was separated by washing with alcohol at the end of 20 hours (Found: S, 14·85%). The time of initiation of gelling was not changed by the substitution of carbon tetrachloride as solvent; with 10% rubber solutions in either solvent, gelling commenced after 30 minutes.—THE BRITISH RUBBER PRODUCERS' RESEARCH ASSOCIATION, 48, TEWIN ROAD, WELWYN GARDEN CITY, HERTS. [*Received, November 24th*, 1944.]

The Oxidation of 1 : 1-*Diphenylethylene with Perbenzoic Acid.* By G. T. NEWBOLD and F. S. SPRING.

BRADSHER (*J. Amer. Chem. Soc.*, 1944, **64**, 45) has reported that treatment of 1-phenyl-1-(2′-diphenylyl)ethylene with an excess of perbenzoic acid gives a neutral "dioxide," $C_{20}H_{14}O_2$, m. p. 111—112°, which, when heated with a variety of reagents, suffers dehydration to give 9-phenylphenanthr-10-ol: the name "dioxide" does not imply any constitutional significance. We record herewith our experience with the oxidation of 1 : 1-diphenylethylene with perbenzoic acid, a reaction first studied some years ago by one of us.

Oxidation of 1 : 1-diphenylethylene with an excess of perbenzoic acid in chloroform gave a 13% yield of a crystalline compound, $C_{21}H_{18}O_3$, m. p. 154—156°, alkaline hydrolysis of which produced a mixture of 1 : 1-diphenylethylene glycol and benzoic acid. The compound, m. p. 154—156°, is therefore a monobenzoate of 1 : 1-diphenylethylene glycol and, since it is recovered unchanged after heating with acetic anhydride, it is characterised as 1-*hydroxy*-2-*benzoyloxy*-1 : 1-*diphenylethane*. The formation of 1 : 1-diphenylethylene glycol monobenzoate from 1 : 1-diphenylethylene is analogous to the preparation of ergostadienetriol monobenzoate by the action of perbenzoic acid on ergosterol (Windaus and Lüttringhaus, *Annalen*, 1930, **481**, 127; see also Böeseken and Elsen, *Rec. Trav. chim.*, 1929, **48**, 363).

Treatment of 1 : 1-diphenylethylene with perbenzoic acid (1 mol.) in chloroform, followed by distillation of the product, gave diphenylacetaldehyde in a minimum yield of 35%. The monobenzoate, m. p. 154—156°, was not obtained in this experiment, nor was it possible to isolate the intermediate 1 : 1-diphenylethylene oxide, which according to Klages and Kessler (*Ber.*, 1906, **39**, 1753) has m. p. 59° and is isomerised to give diphenylacetaldehyde on distillation.

1-*Hydroxy*-2-*benzoyloxy*-1 : 1-*diphenylethane.*—1 : 1-Diphenylethylene (15 g.) was dissolved in a chloroform solution of perbenzoic acid (1000 c.c. containing 28·3 g. of $C_6H_5{\cdot}CO_3H$ as estimated by iodine titration) and kept at 0—5° for 16 days; estimation of the perbenzoic acid content of the solution and comparison with a blank then showed that 1·3

atoms of oxygen had been absorbed. The solution was washed with aqueous sodium bicarbonate, largely concentrated, diluted with ether, again washed with sodium bicarbonate solution and with water, and dried (sodium sulphate). After concentration to small bulk, the solution deposited fine needles (3·2 g.), and a further crop (0·25 g.) was obtained from the mother-liquor by concentration and cooling. After four crystallisations from methanol this gave the *monobenzoate* as needles, m. p. 154—156°, insoluble in water and very soluble in chloroform and in ether [Found: C, 78·9, 79·0; H, 5·65, 5·8; *M*, 319 (Rast); active hydrogen, 0·47%. $C_{21}H_{18}O_2$ requires C, 79·2; H, 5·7%; *M*, 318; 1 active hydrogen, 0·31%]. The monobenzoate was recovered unchanged after refluxing (*a*) for 16 hours with alcoholic phenylhydrazine solution, (*b*) for 24 hours with alcoholic hydroxylamine solution, and (*c*) for 1 hour with acetic anhydride. It gave a light yellow coloration with concentrated sulphuric acid (according to Zerner and Goldhammer, *Monatsh.*, 1929, **53–54**, 485), diphenylhydroxyacetaldehyde gives a red colour).

The monobenzoate (0·25 g.) was refluxed with N-methanolic potassium hydroxide (10 c.c.) for 1 hour, the solution diluted with water (4 vols.), and the crystalline solid collected. Recrystallisation from hot water gave 1 : 1-diphenylethylene glycol as fine needles, m. p. 120—121° (Paal and Weidenkaff, *Ber.*, 1906, **39**, 2063, give m. p. 121°) (Found: C, 78·8; H, 6·6. Calc. for $C_{14}H_{14}O_2$: C, 78·5; H, 6·5%). The aqueous alkaline filtrate was extracted repeatedly with ether, and the aqueous layer concentrated to a small bulk (reduced pressure); acidification with hydrochloric acid gave benzoic acid, m. p. and mixed m. p. 121°.

Diphenylacetaldehyde.—1 : 1-Diphenylethylene (20 g.), dissolved in a chloroform solution of perbenzoic acid (500 c.c. containing 15·52 g. of $C_6H_5{\cdot}CO_3H$), was kept at 0—5° for 7 days; the solution then gave a negative test for perbenzoic acid. The mixture was treated as described in the previous experiment, but no solid product could be isolated. Distillation of the product (mobile oil) gave the following fractions: (1) b. p. 95—110°/0·6 mm., (2) b. p. 115—123°/0·8 mm., (3) 4·1 g., b. p. 123—127°/0·8 mm., residue (5 g.). Fraction (3), when treated with aqueous-methanolic semicarbazide acetate solution, gave (in very good yield) a semicarbazone which separated as felted needles from light petroleum (b. p. 60—80°), m. p. 160—161° (Found: C, 70·7; H, 5·75; N, 16·6. Calc. for $C_{15}H_{15}ON_3$: C, 71·1; H, 6·0; N, 16·6%), not depressed by diphenylacetaldehyde semicarbazone, m. p. 160°. The authentic diphenylacetaldehyde was prepared by the action of dilute sulphuric acid on hydrobenzoin at 170° (Weise, *Annalen*, 1888, **248**, 38) and had b. p. 122—126°/1·7 mm.

Fractions (1) and (2) were combined (10·2 g.) and redistilled, giving two further fractions: (*a*) b. p. 97—102°/0·5 mm. (5·45 g.) and (*b*) b. p. 117—121°/0·5 mm. (3·45 g.). Fraction (*b*) consisted of diphenylacetaldehyde, characterised by the formation of its semicarbazone (felted needles from light petroleum, m. p. and mixed m. p. 160°). Fraction (*a*) readily decolourised bromine water and was probably mainly unchanged 1 : 1-diphenylethylene.—THE UNIVERSITY, MANCHESTER. [*Received, November 28th*, 1944.]

Diffraction Methods in Modern Structural Chemistry.

THE TILDEN LECTURE, DELIVERED BEFORE THE CHEMICAL SOCIETY IN LONDON ON JANUARY 18TH, 1945, AND AT BRISTOL UNIVERSITY ON FEBRUARY 8TH, 1945.

By J. MONTEATH ROBERTSON.

IN his Tilden Lecture last year, Thompson [1] described the application of infra-red measurements to chemistry; this year I wish to go to the other end of the spectrum and deal with an entirely different method. In *X*-ray or electron-diffraction experiments we usually try to build up a picture of the object under investigation by recombining the waves which it scatters. If the object is much smaller than the wave-length, it is well known that we can at best get a blurred picture. Detail on a finer scale than the wave-length is lost, and hence arises the necessity for using short waves. However, we have this much in common with the subject of last year's lecture: in both cases an attempt is made to use as delicate a probe as possible to explore the structure of the molecule. In infra-red radiation we have a delicate energy probe, for the longer the wave-length the smaller is the energy quantum. In *X*-rays or electron waves, on the other hand, we have a delicate measuring rod for ascertaining interatomic distances and other structural data in a rather direct manner.

I. DIFFRACTION METHODS.

It would be out of place here to attempt any detailed account of diffraction methods.[2] We are concerned rather with their application to problems of chemical interest; but something should be said about their present scope and limitations and also about possible future developments. With regard to problems of molecular structure, two main methods have been very extensively developed and employed: electron diffraction, applied to what are effectively single molecules in the gaseous state; and *X*-ray diffraction, applied to crystals. Until recently each of these methods has been confined to a considerable extent to its own particular province. The electron method is most easily applied to gases or to easily volatile substances, and these are just the ones from which it is most difficult to prepare and preserve the well-formed single crystals that are necessary for a detailed study by the *X*-ray method. Between them, therefore, these two methods have covered or can cover nearly the whole field which is of interest in structural chemistry. Where there has been overlap the results have generally been concordant.

When we look a little more closely at these methods we find that the observational data from which the analysis proceeds differ very much in the two cases. In the electron method we get a number of rather minor gradations of intensity on the continuously receding background of the photographic film. But the human eye is a better instrument than most photometers, and by means of what Sutton calls a "singularly impressive optical illusion" a number of well-defined bands can be seen whose relative positions and intensities can be estimated. Quantitative intensity measurements are rather out of the question, and have seldom or never been employed, although improvements in technique may make this possible. For very simple structures, involving one or two parameters, these meagre data are sufficient for a complete and very accurate solution, for the method is very sensitive. Unfortunately, however, as the complexity of the structure increases, the available observations do not multiply in like proportion.

With the *X*-ray crystal method we appear to be in a much happier position. Again, the diffracted beams are generally recorded on photographic films; but this time we can, if we wish, get discrete spots instead of circular bands, and these spots can be related to the angular setting of the crystal. Their positions can be measured accurately to one part in a thousand, or even much better if we care to take the necessary trouble. Their intensities can also be measured, both relatively and absolutely, with an accuracy which depends mainly on the type of photometer or other instrument available.[3] Background scattering is again the limiting factor, but it does not worry us unduly until the method is pushed to the extreme regions of very small or very large angles of incidence. Most important of all, the number of independent measurements which we can make increases with the complexity of the structure under review. Thus, if the unit of structure contains about 10 atoms of carbon, nitrogen or oxygen, together with an appropriate number of hydrogen atoms, then with copper radiation ($\lambda = 1{\cdot}54$ A.) there will be over 500 possible reflections, and we should be able to make intensity measurements on most of them; but if the structure is more complicated and contains 100 such atoms, then about 5000 possible reflections will be available for observation. We have therefore the possibility of making about 50 observations per atom of the structure. Further, we can in principle increase this number as much as we please by using shorter wave-lengths, although in practice background limitations and other difficulties would soon be encountered. So far as I know, this extreme wealth of data has never been fully employed in any structural investigation, with the possible exception of a few elementary substances. One of the most promising and most interesting lines of development undoubtedly lies in the more complete utilisation of these data for the purpose of making really detailed and exact structural analyses.

The comparison so far made between the electron diffraction and the *X*-ray crystal method may appear unfavourable to the former, but our treatment has been superficial because we have not yet considered the nature of the problem which presents itself for analysis in the two cases. For diffraction by gas molecules, this problem is in some ways much simpler than the corresponding crystal problem. The gas molecules are widely separated, and scatter independently. The result can be calculated by treating a single molecule and averaging

over all possible orientations. It is thus possible to set up a model for any molecule, and test it directly by comparing the observed and the calculated diffraction patterns. The parameters can be varied systematically until the best agreements are found.

With a crystal we cannot do this. The molecules or structural units co-operate in scattering, and the whole essence of the experiment is to take advantage of this co-operation in order to build up diffracted or " reflected " rays which are strong enough to measure or record. We must therefore take account of the relative positions of the molecules in the crystal, their distances apart and mutual orientation. If we can work the problem out, we are rewarded with all this additional information about intermolecular distances, information which is beyond the reach of the gas-diffraction experiments; but it makes the problem very much more complex : it is no longer possible to set up a simple model for the molecule and carry out a direct test, for every such model would have an infinite number of different orientations, all of which would require to be tested before that particular model could be either established or eliminated.

The nature of these two different problems becomes very clear if stated in terms of the so-called " direct " methods of analyses which are available in the two cases. The electron scattering $I(s)$ can be represented by the integral

$$I(s) = \kappa \int_0^\infty (r^2 D(r)/s^4)[(\sin sr)/sr]\mathrm{d}r$$

where $r^2D(r)$ represents the product of scattering powers in all volume elements at the distance r apart; s is a function of the scattering angle. This integral can be inverted to give

$$D(r) = \kappa' \int^\infty s^6 I(s)[(\sin sr)/sr]\mathrm{d}s$$

from which $D(r)$, the radial distribution function of the scattering matter, can be calculated from the observations.[4] If the structure consists of atoms, and if most of the scattering takes place at or near the nuclei, then maxima in $D(r)$ correspond to interatomic distances. The complete function represents the superposition of all the interatomic distances in the molecule, and so in principle at least it presents in a very concise form all the information provided by the diffraction pattern.

In crystal-structure work the methods of Fourier analysis,[2b] and in particular Patterson's method, are very similar. The structure amplitude F_{hkl} for any crystal plane (hkl), the absolute value of which can be obtained from the observed intensity of the diffracted beam, is given by the triple integral

$$F_{hkl} = \kappa' \int_0^a \int_0^b \int_0^c \rho(xyz) \exp 2\pi i(hx/a + ky/b + lz/c)\mathrm{d}x\mathrm{d}y\mathrm{d}z$$

where $\rho(xyz)$ is the density of scattering matter at x, y, z; a, b, and c are axial lengths, and hkl Miller indices. A somewhat similar inversion gives the density of scattering matter in terms of the structure amplitudes as

$$\rho(xyz) = \kappa' \sum_{-\infty}^{+\infty} \sum_{-\infty}^{+\infty} \sum_{-\infty}^{+\infty} F_{hkl} \exp - 2\pi i(hx/a + ky/b + lz/c)$$

only in this case the triple series is the correct representation. In the electron-diffraction problem a series is generally used for convenience, but the integral is the correct form. The difference arises from the essentially periodic nature of the crystal. It will be noted also that in the crystal the complete expressions are always triple integrals or triple series because the orientation is fixed and we can explore the structure in three dimensions.

The X-ray crystal problem, however, is not really so simple as this. The F_{hkl} as defined above is a complex quantity, with an amplitude and a phase constant, and the observed intensities in general only enable us to calculate the amplitudes. If we confine ourselves to these observed quantities, Patterson [5] showed that we can calculate a function $\mathrm{A}(uvw)$ from them which is given by the analogous expression

$$\mathrm{A}(uvw) = \kappa'' \sum_{-\infty}^{+\infty} \sum_{-\infty}^{+\infty} \sum_{-\infty}^{+\infty} F^2_{hkl} \exp 2\pi i(hu/a + kv/b + lw/c)$$

Lines joining the origin to peaks in this function give interatomic vectors, and the complete function thus represents the superposition of all the interatomic vectors in the crystal, which, of course, include the vectors between the atoms of adjoining molecules as well as those within the molecule itself. Like the radial distribution function for electron diffraction, the Patterson function again presents in a concise form all the direct information about interatomic distances which is provided by the diffraction pattern.

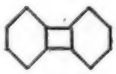
The information obtained from the crystal gives a picture of the structure in three dimensions, and so it is much more detailed than that provided by the gas-diffraction experiments. Nevertheless, in both cases, as soon as we pass beyond the simplest structural units containing three or four atoms, the direct methods of analysis tend to break down because of the complexity of the resulting diagrams and the difficulty of resolving separate peaks. In general it is found necessary to resort to the more indirect but more critical tests of trial and error methods based on the testing of preconceived models of the structure under investigation, and, as

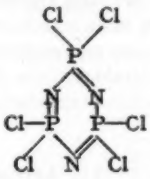
we have already seen, the gas-diffraction method enjoys a great advantage here, because scattering from the molecule is automatically averaged over all possible orientations. With a crystal we may predict the interatomic vectors of any molecule, but the vectors between the atoms of adjoining molecules, which are intermingled with these, are usually much less easy to predict.

This greater simplicity of the gas-diffraction method is reflected in the results already achieved. In its own field it has probably led to a larger number of accurate determinations of interatomic distances than the crystal method. Particularly important for structural chemistry is the way in which it can be employed to compare long series of closely similar compounds, *e.g.*, the work on the chloro- and fluoro-methanes,[6] and on the chlorobenzenes [7] by Brockway and Palmer, and the recent work on halogen derivatives of tin, arsenic, and nitrogen by Skinner and Sutton.[8] With more complicated molecules the method is, of course, limited by the comparative meagreness of its data, but with recent improvements in technique some very striking results

(I.) $CH_2{\cdot}C{\equiv}C{\cdot}CH{:}CH_2$

(II.)



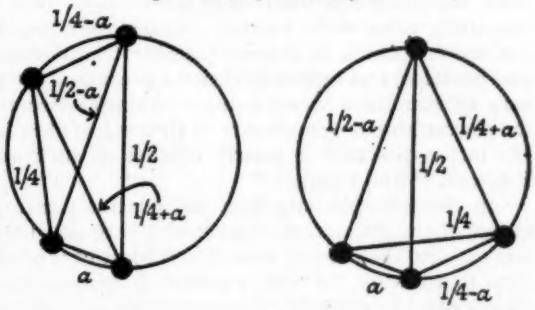


(III.)

have been obtained, in the direction of checking and testing structures. The recent very interesting work by Schomaker and others on the hitherto doubtful structures of pirylene (I) [9] and diphenylene (II),[10] and the full structural determination by Brockway and Bright [11] on the trimer of phosphonitrile chloride (III), are significant examples. If further refinements of the method can be achieved, to give still more detailed diffraction patterns, it seems quite possible that the gas-diffraction method may rival the crystal method in dealing with moderately complex structures. The comparative speed and simplicity of its application are also great advantages.

FIG. 1.

Homometric pair (4 points) with one variable parameter (Patterson).[13]



In comparing these two methods, one final question should be considered. If, in any investigation, excellent agreement is finally obtained between the observed diffraction pattern and the calculated intensities, does this constitute a unique solution of the problem? For gas-diffraction experiments the answer is almost certainly no if the structure contains more than two or three atoms. Even four atoms in general positions involve 12 parameters, which is probably about as great as the number of diffraction maxima which can be observed on the photograph. The process is rather one of showing that a certain assumed model is compatible with the experiments and that other slightly different models lead to inconsistencies. The testing and eliminating of various molecular models is a most important and essential part of the analysis.

In the *X*-ray crystal method we have seen that the number of observed diffraction maxima is very great. In single-crystal work it can always be made very much greater than the number of parameters involved in the structure, even when the atoms are placed in their most general positions. It might then be thought that, once good agreements are obtained between the observed and the calculated values throughout the whole range of the intensities, the structure so determined would constitute a unique solution of the problem.* This is perhaps usually the case but it is by no means always necessarily so. The problem may contain inherent ambiguities which no amount of accurate intensity data alone will solve. The first evidence of this state of affairs in a special case was obtained by Pauling and Shappell,[12] and recently the mathematics of the general one-dimensional problem has been studied by Patterson.[13] He finds that various periodic distributions of points along a line may have the same vector distance set, and that consequently they will give rise to the same *X*-ray diffraction pattern. Such sets of points are termed "homometric." A linear periodic distribution is conveniently represented by plotting the points on the circumference of a circle, and one such homometric pair for four points with one variable parameter is shown in Fig. 1. There is difficulty in developing any general mathematical theory for this problem, and only special cases have so far been investigated. The easiest examples are obtained by arranging the points at r of the n vertices of a regular polygon, and out of 2664 "cyclotomic" sets examined in this way Patterson has found 390 homometric pairs, 7 sets of homometric triplets, and 3 sets of quadruplets. These results are very significant because they show that, even if perfect agreements are obtained between all the calculated and observed *X*-ray intensities, the result may not constitute a unique solution to the problem.

* If the problem is treated as a continuous distribution of scattering matter, without the fundamental assumption that it is concentrated into a limited number of atoms, then it is easy to show that there are always an infinite number of solutions. These may be obtained by assigning arbitrary values to the unknown phase constants, and evaluating the appropriate Fourier series.

In view of this, one may be inclined to regard the outlook rather pessimistically, but it should be emphasised that the real question to be asked about any diffraction problem is whether a unique solution is possible *in terms of reasonable structures*. In practice this is the question always put when structures are analysed in terms of preconceived molecular models. It is important, too, that the solution be supported by other kinds of physical evidence, such as may be furnished by optical and magnetic properties, dipole-moment measurements, etc. All these various lines of evidence should agree and converge before we finally accept a structure as being true.

It should also be emphasised that the above discussion of the *X*-ray problem refers to the general case where complete ignorance of the relative phase constants of the diffracted beams is assumed. In practice, this gap in our knowledge can sometimes be overcome. In the phthalocyanine structures [14] a method was developed for determining the phase constants directly by the comparison of members of an isomorphous series. Again, the " heavy atom " method for settling the phase constant problem has often been used,[15] and promises to become increasingly important. In such cases the results are free from the possibility of such ambiguities as those mentioned above, and they do represent unique solutions. In the most favourable cases, such as that represented by the metal-free phthalocyanine structure, the solution obtained does not even involve the elementary assumption that the molecule is composed of discrete atoms.

II. Application to Molecular Structure.

Bonds between Like Atoms.

Since their inception about 30 years ago, diffraction measurements have been responsible for transforming a large part of both the subject matter and the theory of chemistry. We can hardly imagine what the subject was like when the structures of simple substances like diamond, graphite, and rock-salt were still unknown. With the successful analyses of more complicated structures like the silicates, whole new chapters of inorganic chemistry came to be written. Later, from about 1930, the subject began to branch in two main directions. On the one hand, it became possible to investigate still more complicated structures like cellulose, rubber, and proteins, and in this direction a great deal of progress has been made. On the other hand, it became necessary to examine a larger number of simple structures more accurately to provide a sound experimental basis for the striking developments of theoretical chemistry. The very great part played by diffraction methods in the latter direction is clearly evident in such authoritative reviews of the subject as have been given by Sidgwick [16] and Pauling.[17]

In these simple structures the relative positions of the atoms are usually well known to chemistry; the object of the diffraction experiments is to provide accurate information on interatomic distances and valency angles. At the present time this subject of interatomic distances is rather more suited to a general discussion than to a lecture, for after a period of reasonable stability, when definite rules were formulated, the number of exceptions has gradually increased until now the whole subject is again more or less in the melting pot. This is probably a good thing, because we hope that it will ultimately mean a further advance. All I can do at present is to provide a few rather scanty notes on the position.

About 10 years ago Pauling and Huggins [18] formulated a table of covalent radii which were intended to be applicable to normal structures when the bonds were largely covalent, like those in ethane, chlorine, or carbon tetrachloride. For other valency configurations, such as pure double and triple bonds, other values of the radii were employed. These empirical values were found to be extremely useful in predicting the structures of simple molecules and crystals, and also for drawing attention to special structures where the observed distances differed from the predicted values. Such special cases could usually be explained in terms of resonance, and, in fact, the observed departures from normal distances provided a method for estimating rather accurately the contributions of various postulated structures to the normal state of the molecule.

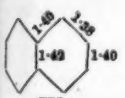
If we confine ourselves first to the case of bonds between like atoms, the process appears to be fairly reliable. By far the largest and most important group concerns bonds between carbon atoms, for these constitute the main framework of organic chemistry. The normal covalent radii for single, double, and triple carbon bonds are 0·77, 0·67, and 0·60 A., derived from measurements on diamond and numerous aliphatic compounds, on ethylene and on acetylene. In practice we find C–C distances which range practically all the way from 1·34 A. (double bond) to 1·54 A. (single bond), and these can be interpreted as representing various states of resonance between single- and multiple-bonded structures. For instance, in benzene, the C–C distance is found to be about 1·39 A., and if we consider the contributions of the two Kekulé structures only, this distance will correspond to a state of 50% double-bond character. In graphite we have to consider many indefinitely extended structures of the type $\overset{C}{\underset{C}{>}}C{=}C$, which gives a 33% double-bond character, and the corresponding distance is now 1·42 A. The amount of double-bond character can be estimated from the empirical curve of Pauling, Brockway, and Beach,[19] which is obtained by plotting these distances against the corresponding bond character.

Some familiar types of conjugation for which reasonably accurate measurements are now available are listed on p. 263, the observed C–C distance referring to the " single bond " between the multiple bonds or benzene rings.

Type.	Compound.	Measured C–C distances, A.	Double-bond character, %.*
	Butadiene [20]	1·46 ± 0·03	18 ± 10
	*cyclo*Pentadiene [20]	1·46 ± 0·03	18 ± 10
	Phenylethylene, Stilbene [21]	1·44 ± 0·02	25 ± 7
	Diphenyl [22]	1·48 ± 0·04	13 ± 12
	p-Diphenylbenzene [22]	1·46 ± 0·04	18 ± 12
	Vinylacetylene, Pirylene [9]	1·42 ± 0·03	25 ± 12
	Tolan	1·40 ± 0·02	33 ± 8
	Diacetylene [25]	1·36 ± 0·03	44 ± 13
	Dimethyldiacetylene [25]	1·38 ± 0·03	34 ± 13
	Cyanogen [25]	1·37 ± 0·02	33 ± 10

* For structures involving triple bonds a correction of 0·02 A. is applied for each triple bond, to allow for a small postulated contraction in the covalent radius.

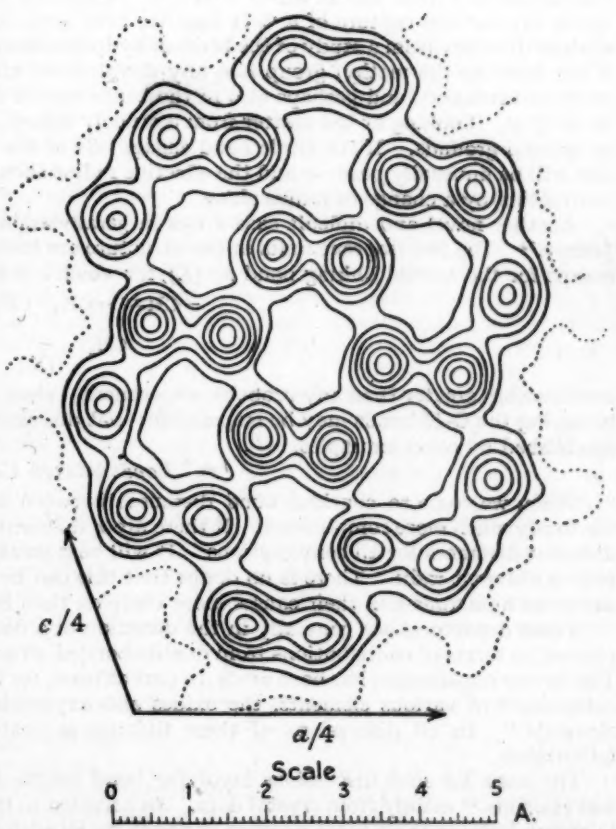
When we wish to make quantitative predictions of the bond lengths in such systems, more accurate calculations are necessary. These have been carried out for a number of cases by Lennard-Jones,[26] Penney,[27] and Coulson [28] by both the "molecular orbital" and the "electron pair" method. A "bond order" can be derived which is linearly related to the bond energy, and then bond lengths may be obtained by interpolation from the standard values in diamond, graphite, ethylene, and acetylene. Calculated in this way, the length of the connecting "single" bond in butadiene comes out at 1·43 A., and in phenylethylene at 1·45 A., figures which are in quite good agreement with the observed values. For the condensed-ring aromatic hydrocarbons similar calculations can be made, and the results indicate certain small variations in the C–C distances for different bonds. The calculated results for naphthalene are shown in (IV). The average, 1·40 A., is in excellent agreement with the measured value of 1·41 A. The individual variations are rather beyond the reach of experiment at present, although there is some indication that the central bond may be slightly larger than the others.



(IV.)

The high symmetry of the coronene molecule makes it an interesting one to study in this connection. The crystal measurements are not yet very complete, but the preliminary results [29] which have been obtained (Fig. 2) indicate that the average C–C distance is slightly greater than in benzene (1·39 A.) and probably nearer the graphite value of 1·42 A.

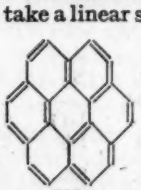
FIG. 2.

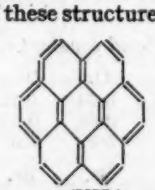


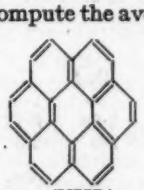
Electron density map for coronene. The plane of the molecule is inclined at about 45° to the projection plane, with consequent distortion of the hexagonal symmetry.

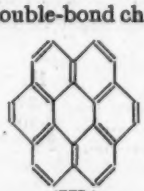
Five groups of stable valency-bond structures (V)—(IX) can be written, which contain the number of individuals shown. If we take a linear sum of these structures and compute the average double-bond character

(V.)
4 Structures.


(VI.)
6 Structures.


(VII.)
3 Structures.


(VIII.)
6 Structures.


(IX.)
1 Structure.

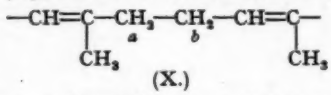
we find, for the 18 outer bonds, 43%; for the 6 "spokes," 40%; and for the 6 inner bonds, only 30% double-bond character, as compared with 50% in benzene and 33% in graphite. The overall average for coronene is

40%, which is nearer to graphite than to benzene. These calculations are rather crude, but they may have some measure of success for this particular molecule because of its high symmetry. Coulson [30] has recently examined the coronene problem in detail by the molecular orbital method, and has calculated the bond energies and bond orders. He finds the mean length of all the bonds to be 1·406 A., with the central bonds 1·418 A., compared with 1·417 A. (assumed) in graphite and 1·389 A. (assumed) in benzene.

The theoretical calculations for systems containing mainly one kind of atom thus appear to be capable of considerable refinement. It should be emphasised that the diffraction measurements on bond lengths at present available are not nearly accurate enough to provide a really critical test of the theories. For the systems we have been discussing, the most interesting variations all lie within the limits of experimental error, which are usually about $\pm 0{\cdot}02$ or $\pm 0{\cdot}03$ A. in the best determinations, and may be much greater in some cases. There is a great deal of scope for future refinement in this direction.

In other cases the measurements are quite accurate enough to reveal large departures from the expected distances which are difficult to explain in terms of resonance with multiple-bonded structures. Here there would appear to be scope for further development of the theories. For example, in the methylacetylenes the C–C single bond to the methyl group shows a contraction of about 0·07 or 0·08 A.[25, 31] In methyl cyanide the contraction is rather less at about 0·05 A.[32] Resonance with double-bond structures such as $\overset{+}{\mathrm{H}}\mathrm{CH}_2{=}\mathrm{C}{=}\overset{-}{\mathrm{C}}\mathrm{H}$ which involve the rupture of a C–H link has been proposed to explain the contraction, but there is evidence against this view from a study of the heats of hydrogenation of acetylene and its methyl derivatives.[33] Further, if the bond to the methyl group had any double-bond character, we might expect some evidence of this in restricted rotation, and perhaps also in the behaviour of the methyl hydrogens, but such evidence appears to be lacking. Looking at the matter from a crudely chemical point of view, one might expect some contraction on general grounds. If the triple bond engages six of the electrons on one side of the carbon atom, the other side will be unusually positive and the effective radius should decrease; but it is very difficult to explain all the contraction by a change of radius alone.

Another novel and difficult case arises in geranylamine hydrochloride, recently studied by Bateman and Jeffrey.[34] The two isoprene units in this structure are found to have normal configurations and bond distances except for the central linking bond *ab* (X), for which a contraction of 0·10 or 0·09 A. is reported. This seems



(X.)

considerably greater than any probable experimental error, and it is suggested that a hyperconjugation process involving the C–H bonds may be responsible; but discussion should be deferred until the result can be further established by other examples.

Bonds between Unlike Atoms.

When we come to consider bond distances between atoms of different kinds, the problems arising are obviously much more complicated. If there are n different kinds of atom, we might in general expect about $\frac{1}{2}n^2$ different distances for all combinations. It will be a great simplification if we can derive these distances from only n different radii. There is no doubt that this can be done approximately, but departures from the rules are more numerous and their causes more complex than before.

These departures are generally in the direction of a decrease from the predicted values, which may be explained in terms of contributions from double-bonded structures, or by the partly ionic character of the bonds. The former explanation has been made, in part at least, for the shortened bond distances observed in the halogen compounds of various elements, the oxides and oxy-acids, and in the covalent complexes of the transition elements.[17] In all discussions of these theories accurate measurements of bond distance are of extreme importance.

The basis for such discussions involving bond length are the tables of covalent radii derived by Pauling and Huggins [18] mainly from crystal data. In addition to the ordinary covalent radii, given below, which apply to atoms forming their usual number of bonds (as given by their place in the Periodic Table), there are tables of tetrahedral covalent radii and octahedral covalent radii for use in crystals of these types. The tetrahedral radii do not differ much from the normal covalent radii, which apply to a large variety of compounds including some with considerable ionic character. For true ionic crystals (alkali halides, etc.) quite a different set of ionic radii must be used.

Single-bond covalent radii.

	H.	Li.	B.	C.	N.	O.	F.	Na.	Si.	P.	S.	Cl.	
r [a]	0·37	1·34	—	—	0·74	0·74	0·72	1·54	—	—	—	—	
r [b]	0·30	—	0·88	0·77	0·70	0·66	0·64	—	1·17	1·10	1·04	0·99	
x [c]	2·1	1·0	2·0	2·5	3·0	3·5	4·0	0·9	1·8	2·1	2·5	3·0	
		K.		Ge.	As.	Se.	Br.	Rb.	Sn.	Sb.	Te.	I.	Cs.
r [a]		1·96		—	—	—	—	2·11	—	—	—	—	2·25
r [b]		—		1·22	1·21	1·17	1·14	—	1·40	1·41	1·37	1·33	—
x [c]		0·8		1·7	2·0	2·4	2·8	0·8	1·7	1·8	2·1	2·4	0·7

[a] Value of r as revised by Schomaker and Stevenson.[39] [b] Former value of r due to Pauling and Huggins.[18]
[c] Electronegativity values (Pauling [17]).

There is an enormous mass of consistent evidence in support of the covalent radii, derived mainly from diffraction studies on various compounds. One may mention, as an example, the extensive series of measurements on methyl compounds made by Brockway and Jenkins [35] and others. By subtracting the well-known carbon radius from the observed distances, the radii of the other elements can be obtained, in excellent agreement with the Pauling–Huggins figures.

In spite of all these agreements, however, it has recently become clear that a revision of the long-accepted values is necessary for the three elements nitrogen, oxygen, and fluorine. This arises from recent accurate measurements of what must be regarded as true single bonds between the atoms of these elements in hydrogen peroxide,[36, 37] hydrazine,[37] and fluorine.[38] The distances obtained are O–O = 1·47 ±0·02 A., N–N = 1·47 ±0·02 A., and F–F = 1·435 ±0·01 A., giving radii of 0·74, 0·74, and 0·72 A., respectively. This rather drastic upward revision means that many observed bond lengths for compounds involving these elements are now significantly less than their radius sum, even where no double-bond character is likely to exist. In such cases Schomaker and Stevenson [39] attribute the deviation to the extra ionic character of the bond between the unlike atoms as compared with whatever ionic character there may be in normal bonds between like atoms of the kinds respectively involved. In an attempt to predict the distance r_{AB} from the radii r_A and r_B they employ the empirical relation

$$r_{AB} = r_A + r_B - \beta|x_A - x_B|$$

where x_A and x_B are the Pauling electronegativities for the atoms concerned, and the constant β is given the value 0·09. The deviations are thus found to be proportional to the absolute value of the electronegativity differences. These electronegativities are defined by Pauling [17] in terms of bond energies, and are linearly related to the square roots of the differences between the actual bond energies for unlike atoms A–B and the expected bond energies for normal covalent bonds, the latter being taken as the arithmetical mean of the bond energies for A–A and B–B.

Schomaker and Stevenson have tested this relation fairly extensively. Although it tends to give low values for the bond distances in many cases, they consider that there is enough general agreement to warrant its adoption as a basis for the rediscussion of bond distances between unlike atoms. Much of this rediscussion is presumably still to come, and also further comparisons with more accurately determined distances, so it would be out of place to attempt any adequate review here. We may note, however, that as a result of the revised radii there has been rather a shift of emphasis in regard to explanations of bond contractions. Bond character as expressed by the electronegativity difference becomes more important, perhaps at the expense of bond multiplicity theories.

This is particularly the case with halogen compounds, and attention should be directed to the recent interesting work of Skinner and Sutton [8] on the halogen derivatives of various elements. It is a very general phenomenon that, as the number of halogen atoms attached to some central atom is increased, so the bond length progressively contracts. This contraction is small but fairly definite for a large variety of atoms. Any straightforward explanation of this in terms of either multiple character of the links or electronegativity differences seems difficult; but each substitution by halogen will tend to put some positive charge on the central atom, which in turn will tend to decrease its radius. The countereffect on the halogen may tend to increase its radius, but this effect will decrease progressively as further halogens are added. There will also tend to be a net increase in the attractive forces during this process of halogen addition, and so on both counts we should expect a small progressive decrease in bond distances. It is to be hoped that a more quantitative expression of this theory will be developed.

III. Possible Extensions of the Diffraction Methods.

Although, as we have seen, distance measurements are extremely important, it is clear that they are not in any way a sufficient basis for full and detailed discussions of the structure and nature of bonds. What we require most of all is a detailed picture of the electron distribution in bonds of various kinds. Dipole-moment measurements can furnish much valuable information in this direction,[40] but we should like to be able to supplement this by other and if possible more detailed information derived from the study of individual linkages.

In principle, diffraction measurements can furnish information of this kind, if they are pushed far enough. The complete solution of a crystal structure is expressed by a map which gives the electron density at every point in the structure. It is true that this information is not, in general, furnished directly by the experimental measurements of structure amplitudes. We have seen that these quantities lead only to the corresponding vector diagram, which is frequently too complicated to be of direct assistance. Nevertheless, once the structure has been roughly established, by whatever means, then the true electron-density maps can be calculated and further and further refined by successive approximations.

We have also seen that in hardly any case has full use yet been made of all the available data in *X*-ray crystal analysis. Results regarding atomic positions are usually obtained from two-dimensional projections of the structure, which utilise only about $n^{\frac{1}{2}}$ of the n available observations. A partial three-dimensional analysis is sometimes made for complicated structures for the better location of atoms,[41] but I do not know of any case where it has been carried to the limit, with the full use of quantitative intensity measurements.

Thorough-going analyses of this kind will become necessary if we wish to gain any detailed information about electron distribution. Considerable difficulties are involved in the accurate measurement of intensities

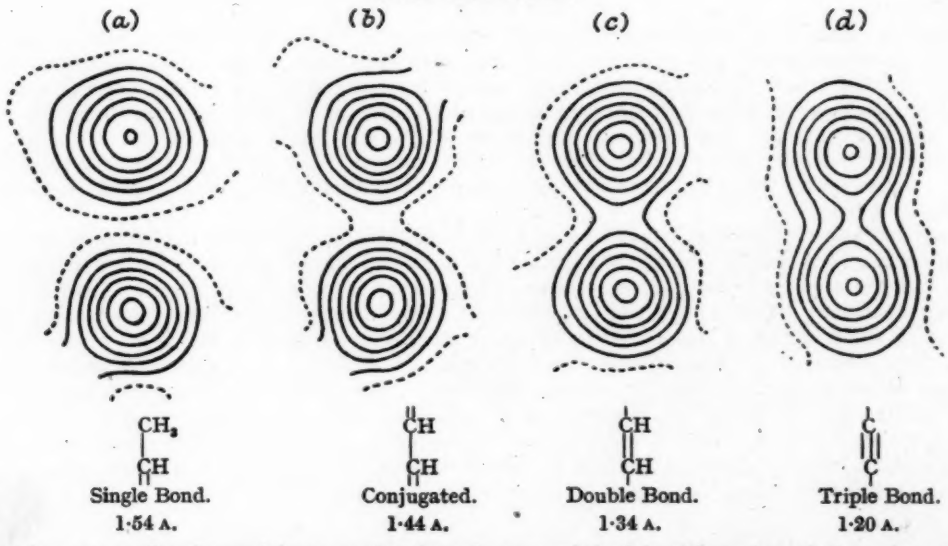
and their correction for various disturbing factors such as the perfection of crystal specimens; also in the calculation of the results and their correction for spurious diffraction effects of various kinds. These difficulties, however, are not fundamental and there is no doubt that they can be overcome, largely by the proper planning and organisation of the research, which will have to be on a fairly large scale.

It is more difficult to say just how much information would be obtained from a comprehensive investigation of this kind. The inner electrons are concentrated in a relatively small space and are the most effective in scattering. Because of this we can determine atomic positions with accuracy. Much of the spread of electron density which we see in contour maps is due to thermal movement of the atoms. At lower temperatures the peaks sharpen and the outer effects diminish. Consequently, it is very difficult to reach conclusions about these outer effects. The situation is rather similar to that which arises when we try to locate light atoms in the presence of heavy ones, and this is difficult in all diffraction experiments.

The presence of hydrogen atoms, for example, has very little effect in *X*-ray crystal analysis and they are usually neglected in the preliminary calculations. In the final representation of the results, however, they probably have some effect, although they tend to become submerged in the outer parts of the carbon atoms. If we examine the contour map for coronene,[29] shown in Fig. 2, which is only a preliminary two-dimensional projection of the structure, we see that there are distinct bulges around every outer carbon atom to which we expect to find a hydrogen atom attached. This is very apparent in the dotted contour line which represents a density of about one electron per A.^{2}. Similar effects have been observed in many other hydrocarbon structures; but I have never directed much attention to these effects in the past because they are obviously far from precise, and they await confirmation from more detailed and exact analyses. The position of the one-electron

FIG. 3.

Carbon–carbon bonds.



density line is very easily changed because the slope is very gradual in this region of the map. Diffraction effects arising from the incompleteness of the Fourier series used, or lack of convergence, have large effects on the position of the dotted line, but evidence is accumulating, and on the whole the coronene hydrogen effect would appear to have some significance.

With regard to electron distribution in the bonds themselves, some fairly detailed work has been briefly reported by Brill and his co-workers.[42] They find that in the sodium chloride crystal the electron density falls to zero between the ions, but that in diamond a small residual density remains between the carbon atoms, which is attributed to the covalent linkage. The latter result may unfortunately be vitiated by uncertainty regarding some of the phase constants, and in general the work appears to require further confirmation. Some interesting intermolecular effects are also reported for hexamethylenetetramine and oxalic acid dihydrate.[43]

In our own analyses there are many bond effects to which attention might be directed, but as in the case of the hydrogen atom, these effects are not precise. Two-dimensional Fourier projections are very misleading with regard to electron-density distribution because the amount of overlapping which is shown between a pair of atoms obviously depends primarily on the angle which the bond between them makes with the projection plane, *i.e.*, the angle from which they are viewed. There may also be atoms belonging to other molecules in the structure which prevent any clear projection of a particular pair. In general, it would be much better to employ sections of three-dimensional syntheses.

However, in special cases normal or nearly normal projections of a particular pair of atoms can be obtained. Fig. 3 shows (*a*) a CH_3–CH= single bond in the sorbic acid structure[44] (C–C distance, 1·54 A.); (*b*) a shortened =CH–CH= bond, situated between two double bonds, in the same structure (C–C distance, about 1·44 A.);

(*c*) one of the sorbic acid double bonds, $-CH=CH-$ (C–C distance, 1·34 A.); (*d*) a triple bond, $-C\equiv C-$, from the tolan structure [24] (C–C distance, 1·19 A.). In each case the bond is tilted at a small angle (12—15°) to the projection plane, which gives an apparent additional shortening of about 3% in the bond length.

The above results are therefore fairly comparable with one another, and it is seen that the electron density between the atoms rises fairly steadily from something under one electron in the single bond to just over four electrons per A.^{3} in the triple bond. (Each contour line represents a density increment of one electron per A.^{3}, the one electron line being dotted.) It is to be emphasised that these are the actual distributions found, and that no correction has been made for the thermal movements of the atoms, which have a very large effect in spreading the observed electron densities.

Calculation shows that the overlapping effect observed in the first three cases is just about the same as would result from bringing pairs of average carbon atoms in these structures to within the specified distances. In the triple bond there appears to be a small additional effect, *i.e.*, the bridge density is a little higher than can be explained by normal overlapping for the given separation of the atoms. However, it is clear that in order to obtain useful information a much better resolution is required, with correction for temperature factor, etc.

Considerable further development appears to be possible in these directions. The gas-diffraction method, too, may be employed, especially when improvements in technique make quantitative intensity measurements possible, particularly in the direction of small angle scattering. This method would have the great advantage of being readily applied to certain very simple and critical types of molecule. In such directions as these we may ultimately hope to gain a far more intimate and detailed view of the structure of molecules.

This account of the part played by diffraction methods in modern chemistry has necessarily been very inadequate and confined almost entirely to covalent bond types. No reference has been made to the large amount of exact work on ionic crystals and metals, or to general stereochemical problems. Sidgwick and Powell's recent paper [45] shows very clearly the great part played by diffraction methods in the latter direction. Again, no reference has been made to the large and growing amount of work on the weaker type of intermolecular bonds, on the structure of molecular compounds, hydrogen bridges, surface structures, and so on. Indeed, a complete survey of the scope of the subject at the present time would mean nothing less than a complete survey of practically the whole of modern chemistry.

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Non-benzenoid Aromatic Hydrocarbons.

THE TILDEN LECTURE, DELIVERED IN LONDON ON OCTOBER 19TH, 1944, AND IN EDINBURGH ON FEBRUARY 23RD, 1945.

By WILSON BAKER, M.A., D.Sc.

A TILDEN Lecturer is expected to review the progress in some branch of chemical science. In dealing with the present position of our knowledge of the chemistry of the non-benzenoid aromatic hydrocarbons the Lecturer is aware that there are few outstanding recent developments to report. A survey of these compounds at the present time may, however, be of value, as they are of considerable practical and theoretical interest, and this interest is reflected in the number of papers published during the last few years dealing with the chemical and physical aspects of such organic systems. The literature of the non-benzenoid aromatic hydrocarbons contains some material that is of doubtful value, and if part of this account is of a critical character, it is in the hope that thereby a more sound foundation may be laid for future developments.

In discussing the characteristics of benzene in a paper appearing in the *Journal* of the Chemical Society in 1888 (**53**, 888) Sir William Tilden wrote as follows:

> " 1. The six atoms of carbon in benzene form a very stable group, which is not easily broken up by heat or by chemical reagents.
>
> " 2. The carbon atoms are all in the same condition, and the hydrogen is distributed equally among them.
>
> " 3. The carbon atoms are not united together by ethylenic bonds.
>
> " 4. There are three, and only three, disubstitution derivatives."

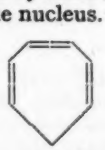
These statements are of equal value to-day as when they were written, though some additions might profitably be made. In the same paper Sir William Tilden, in referring to the Kekulé formula for benzene, pointed out the objection to the use of the same symbol to denote the chemically reactive carbon–carbon bond in ethylene and three of the comparatively inert carbon–carbon bonds in benzene, but he added " Doubtless most chemists have been in the habit of indulging in a mental reservation as to the significance of the double bond in a closed chain. This, however, does not justify the employment of the same symbol to express two different things." This criticism is still effective, and will remain so until a convenient, simple, chemical symbol is adopted to represent the hybrid aromatic bond.

In the absence of this chemical symbol the aromatic formulæ in this lecture will be represented by conventional Kekulé structures, but the mental reservation must be made that these double bonds are not fixed, nor are the compounds tautomeric mixtures of the structures with various arrangements of the valency bonds, but are resonance-hybrid molecules. In these molecules the stability and tendency towards saturation are consequences of this hybrid character, and a molecule may be said to be of aromatic type if it is a cyclic unsaturated compound containing at least two conjugated double bonds in the ring when represented by the conventional symbols, and in which these bonds interact to a greater or lesser extent, thus bringing about a certain stabilisation of the molecule by resonance, which will in consequence be more saturated than if the double bonds were fixed and purely olefinic in character. A benzenoid aromatic compound contains a six-membered ring and the equivalent of three double bonds, as in benzene and pyridine; aromatic compounds not of the benzene type may be described as non-benzenoid.

The degree to which aromatic stability and saturation are developed is represented quantitatively by the resonance energy of the molecule, calculated from the value either of the heat of combustion or of the heat of hydrogenation (Kistiakowsky and co-workers, *J. Amer. Chem. Soc.*, 1935—1939). For benzene this amounts to some 39 kg.-cals. per g.-mol, and for naphthalene to 75 kg.-cals. per g.-mol. With *cyclo*pentadiene (I) and *cyclo*heptatriene (tropilidine) (II) the values calculated from the heats of hydrogenation are only about 3 and 6·7 kg.-cals. per g.-mol. respectively, so these molecules do not appear to possess a greater degree of resonance energy than the corresponding open-chain compounds, which they resemble in their general chemical reactivity. *cyclo*Pentadiene and *cyclo*heptatriene cannot, therefore, be said to be markedly aromatic in type, and a significant degree of aromatic character can only be developed in a molecule if it is more fully conjugated, as in those cases where there are completed cyclic conjugated systems, *e.g.*, benzene.

The present review will deal with the monocyclic *cyclo*butadiene, *cyclo*octatetraene, and the fulvenes; the dicyclic pentalene and azulene systems; and the tricyclic diphenylenes, with an additional note on four-membered rings fused to a benzene nucleus.

(I.)



(II.)

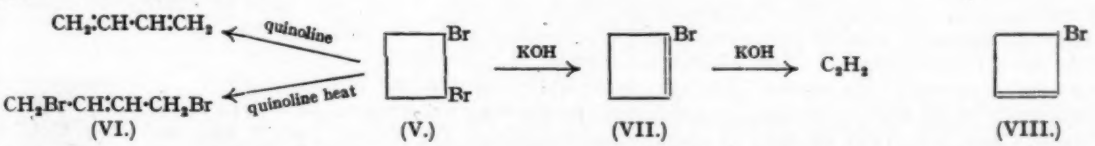
(III.)

(IV.)

The simplest hydrocarbons which might exhibit aromatic stability and properties are *cyclo*butadiene (III) and *cyclo*octatetraene (IV). It is commonly stated in text books of organic chemistry that *cyclo*butadiene is to

instable to exist, and that *cyclo*octatetraene, although capable of independent existence, is quite unlike benzene and behaves as a typical polyolefin. Statements to the same effect are also to be found in papers of a physico-mathematical nature dealing with the structure of benzene, and unless such statements are well founded any conclusions which may be drawn from them may be invalid. It is, therefore, of some importance to examine closely the evidence upon which these statements are based, and an attempt is made to do this in the following two sections.

cyclo*Butadiene*.—Chemical literature contains only one reference to the attempted preparation of *cyclo*butadiene. Willstätter and von Schmaedel in 1905 (*Ber.*, **38**, 1992), by the thermal decomposition of *cyclo*butyltrimethylammonium hydroxide, prepared *cyclo*butene, which was then converted into *cyclo*butene dibromide (V). When (V) was distilled, it gave 1 : 4-dibromo-Δ^2-butene (VI), and when boiled with quinoline, gave a trace of butadiene. *cyclo*Butene dibromide, when heated with potassium hydroxide at 100—105°, gave the stable 1-bromo*cyclo*butene (VII), which reacted further with potassium hydroxide at 210° to give a 30% yield of acetylene.

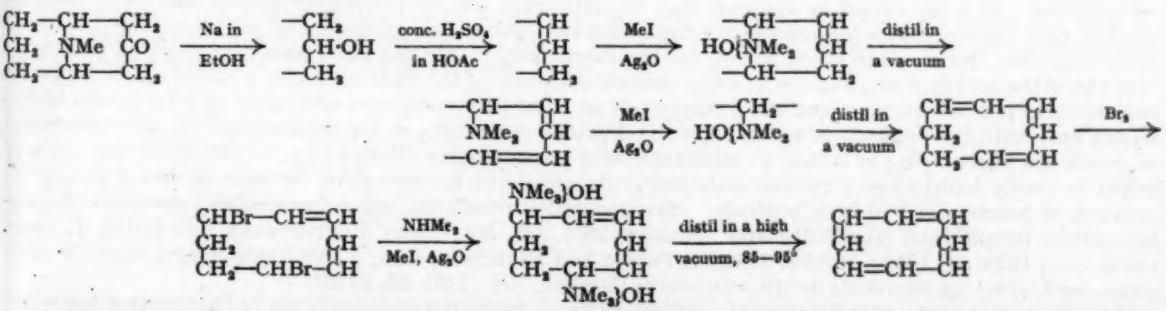


(VI.) (V.) (VII.) (VIII.)

These facts suggest that *cyclo*butadiene is not a very stable compound, but do not prove that *cyclo*butadiene is incapable of existence. From a knowledge of the behaviour of *cyclo*propane and *cyclo*butane and derivatives, the ring systems of which are readily broken, the molecule of *cyclo*butadiene would certainly be expected to be somewhat instable, and, owing to increased angular strain, would doubtless be less stable than *cyclo*butene and *cyclo*butane. In passing from *cyclo*butene to *cyclo*butadiene, however, the increased angular strain might be compensated, at least in part, by resonance interaction between the conjugated double bonds. There is thus a possibility that *cyclo*butadiene might be prepared if the final reaction leading to its formation were of a not too vigorous character, and the most promising line of attack would be to prepare 1-bromo-Δ^2-*cyclo*butene (VIII) (probably by the bromination of *cyclo*butene with *N*-bromosuccinimide; Ziegler, Späth, Schaaf, and Schumann, *Annalen*, 1942, **551**, 80) and to eliminate hydrogen bromide directly or to replace the bromine atom by the dimethylamino-group and proceed by exhaustive methylation. The process of exhaustive methylation has already proved successful in the preparation of the highly strained molecule of *cyclo*propene in 45% yield from *cyclo*propyltrimethylammonium hydroxide at 320—330° (Demjanov and Dojarenko, *Bull. Acad. Sci. Russ.*, 1922, **6**, 297; *Ber.*, 1923, **56**, 2200; Schlatter, *J. Amer. Chem. Soc.*, 1941, **63**, 1733).

A few examples are to be found in the literature of compounds which have been supposed to be derivatives of *cyclo*butadiene or of the *cyclo*butadiene type. Thus Ruhemann and Merriman (J., 1905, **87**, 1383) have described some derivatives of *cyclo*butadiene, but the suggested formulæ are highly speculative and are not supported by adequate chemical evidence. Again, Curtius and Thun (*J. pr. Chem.*, 1891, **44**, 175) suggested that the azine produced from hydrazine hydrate and diacetyl was of the butadiene type, but it was later shown by Zimmermann and Lochte (*J. Amer. Chem. Soc.*, 1936, **58**, 948) to be a polyazine of moderately high molecular weight.

cyclo*Octatetraene*.—The preparation and properties of the hydrocarbon believed to be *cyclo*octatetraene were described by Willstätter in two papers in 1911 and 1913 (Willstätter and Waser, *Ber.*, 1911, **44**, 3423; Willstätter and Heidelberger, *Ber.*, 1913, **46**, 517). The starting material was the pomegranate alkaloid ψ-pelletierine, which contains the *cyclo*octane nucleus bridged by an NMe group. The steps of the preparation are shown in the following scheme:



The final step, the thermal decomposition of the quaternary hydroxide derived from the diamine, was carried out at low pressure and gave the hydrocarbon in 10—20% yield as a pale yellow liquid, b. p. 42·2—42·4°/17 mm., the three analyses of which agreed well with the formula C_8H_8. It was instable on exposure to the air and deposited amorphous flocks (Willstätter and Waser) or resinified (Willstätter and Heidelberger), and, curiously, it exhibited a limited degree of unsaturation. In dilute chloroform solution at −20° it combined with bromine, giving a crystalline dibromide, $C_8H_8Br_2$, which, by the further action of bromine, gave by substitution a

solid, incompletely characterised bromo-dibromide, $C_8H_7Br_3$. With hydrogen bromide it gave a liquid hydrobromide, C_8H_9Br, which did not combine with bromine. Both the hydrocarbon and its dibromide reduced potassium permanganate energetically.

Reduction of the *cyclo*octatetraene with hydrogen and an active platinum catalyst resulted in the slow absorption of four molecules of hydrogen and formation of a hydrocarbon C_8H_{16}, b. p. 39—42°/15 mm., which solidified on cooling and became completely fluid at 6·5°. With the same catalyst and under the same conditions benzene was completely reduced, though slightly more rapidly. The hydrocarbon C_8H_{16} was considered to be *cyclo*octane (m. p. 14°) because on oxidation with nitric acid it gave suberic acid, $HO_2C{\cdot}[CH_2]_6{\cdot}CO_2H$, but details of this important experiment are lacking.

Although many chemists may have wondered if Willstätter's hydrocarbon really was *cyclo*octatetraene, not until 1939 was the validity of his conclusions challenged in print. In that year Vincent, Thompson, and Smith (*J. Org. Chem.*, 1939, **3**, 603) drew attention to the "striking similarity in chemical and physical properties between Willstätter's compound and its derivatives and styrene and its derivatives." This similarity to styrene was again emphasised by Goldwasser and Taylor (*J. Amer. Chem. Soc.*, 1939, **61**, 1260), who stated that styrene had the same specific gravity and showed chemical properties identical with those reported by Willstätter for *cyclo*octatetraene. The widespread interest in *cyclo*octatetraene, undoubtedly stimulated by this suggestion, is shown by the number of independent publications dealing with the subject. In addition to those investigators whose work is specifically mentioned, preliminary experiments have been recorded by Wawzonek (*J. Amer. Chem. Soc.*, 1943, **65**, 859), Bachmann and Hoaglin (*J. Org. Chem.*, 1943, **8**, 300), and Cook, McGinnis, and Mitchell (J., 1944, 290), and Horning (*Chem. Rev.*, 1943, **33**, 96) has suggested that an intermediate in the final step of the synthesis leading to styrene is the benzene derivative $Ph{\cdot}CH(NMe_3{\cdot}OH){\cdot}CH_3$. Although the chemical properties of styrene are undoubtedly very similar to the recorded properties of *cyclo*octatetraene, the physical properties (see Table) are not, in fact, in close agreement, except for the boiling point.

	cyclo*Octatetraene.*		*Styrene.*
B. p.	42·2—42·4°/17 mm.	B. p.	43°/17 mm.
M. p.	−27°	M. p.	−33°
$d_4^{0°}$	0·943	$d_4^{0°}$	0·925
$d_4^{20°}$	0·925	$d_4^{20°}$	0·907
$n_D^{20°}$	1·5394	$n_D^{21°}$	1·5446
Dibromide, m. p.	70—71·5°	Dibromide, m. p.	74°

A different approach was that of Hurd and Drake (*J. Amer. Chem. Soc.*, 1939, **61**, 1943), who criticised several of the assumptions which were made as to the nature of the intermediate products in the conversion of ψ-pelletierine into *cyclo*octatetraene. For example, both the diene and the triene were assumed to be conjugated, the addition of bromine to the triene was regarded as a 1 : 6-addition, and the derived bis-quaternary ammonium hydroxide was again supposed to give the conjugated tetraene. It is now known that bromine does not always add terminally to conjugated systems, and with regard to the decomposition of bis-quaternary ammonium hydroxides, cases investigated by Hurd and Drake showed that conjugated systems by no means always resulted, *e.g.*,

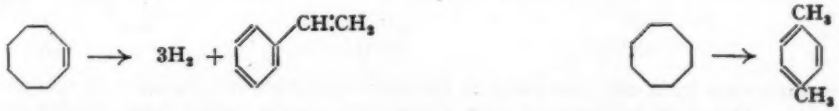
$$\underset{(42—47\%)}{CH_3{\cdot}CH{:}CH{\cdot}CH_3} \longleftarrow CH_3{\cdot}\overset{NMe_3\}OH}{CH}{\cdot}\overset{NMe_3\}OH}{CH}{\cdot}CH_3 \longrightarrow \underset{(53—58\%)}{CH_3{\cdot}CH{:}C{:}CH_2} + CH_3{\cdot}C{\vdots}C{\cdot}CH_3$$

The evidence available makes it impossible to come to any definite conclusion as to the nature of Willstätter's hydrocarbon. On the one hand, its boiling point, ability to resinify, and the formation and properties of the dibromide and hydrobromide, which behave as saturated compounds towards bromine, suggest that it was styrene. It must indeed be assumed that the dibromide and hydrobromide are derivatives of benzene, because on no other reasonable ground can their saturated nature be explained, and of the possible benzenoid compounds the styrene derivatives are by far the most likely.* On the other hand, its physical properties, apart from the boiling point, and the recorded energetic reaction of the dibromide with potassium permanganate indicate that it is not styrene, and the formation of an octahydro-derivative oxidisable to suberic acid is consistent only with the presence of at least some *cyclo*octane derivative, either the conjugated *cyclo*octatetraene or, much less likely owing to strain, a *cyclo*octatetraene containing an allene group. This conflicting evidence might be partly harmonised if *cyclo*octatetraene could yield styrene derivatives by rearrangement during the addition of bromine or hydrogen bromide. This suggestion recalls the somewhat similar conversion of *cyclo*heptatriene (tropilidene) (II) (Willstätter, *Annalen*, 1901, **317**, 204; Conn, Kistiakowsky, and Smith, *J. Amer. Chem. Soc.*, 1939, **61**, 1868; Kohler, Tischler, Potter, and Thompson, *ibid.*, p. 1057) into benzyl bromide (10% yield), by heating its dibromide on the water-bath (Merling, *Ber.*, 1891, **24**, 3122).

It is clear that in the present state of our knowledge no useful purpose can be served by contrasting either the chemical or physical properties of Willstätter's *cyclo*octatetraene with those of benzene, though it is certainly also clear that the *cyclo*octatetraene ring system is much less easy to produce than that of benzene.

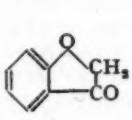
* A dibromide or a hydrobromide of a structure such as that of the cyclic fulvene derivative shown, or its four possible isomerides with various positions of the double bonds, is excluded if it be accepted that reduction of Willstätter's *cyclo*octatetraene gave *cyclo*octane (Barrett and Linstead, J., 1936, 611, find no conversion of 0 : 3 : 3-*bicyclo*octanes into *cyclo*octanes by reduction).

Derivatives of *cyclo*octatetraene do not occur naturally, nor have they been produced by simple reactions in the laboratory, as has benzene and a very large number of its derivatives. That this is due to something more than the usual difficulty of closing an eight-membered ring is shown by experiments with compounds in which the *cyclo*octane structure is already present. For example, Goldwasser and Taylor (*loc. cit.*) attempted the catalytic dehydrogenation of *cyclo*octene over a chromium oxide catalyst at 425°, and obtained in the liquid distillate a 93% yield of styrene, and no trace of any other system absorbing in the ultra-violet region of the spectrum.

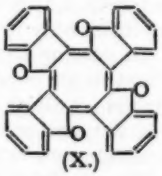


Again Ruzicka and Seidel (*Helv. Chim. Acta*, 1936, **19**, 424) showed that *cyclo*octane and *cyclo*heptane at 440° gave *p*-xylene and toluene respectively, and even in the saturated series eight- and also seven-membered rings rearrange to *cyclo*hexanes. Thus *cyclo*octane at 210° in hydrogen over nickel gave 1 : 1-dimethyl*cyclo*hexane (Willstätter and Kametaka, *Ber.*, 1907, **40**, 957), and *cyclo*heptane at 230° in hydrogen over nickel gave methyl*cyclo*hexane (Ruzicka, *Helv. Chim. Acta*, 1926, **9**, 499).

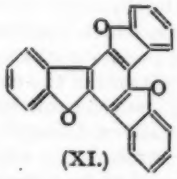
Derivatives of cyclo*octatetraene.* Compounds supposed to be derivatives of *cyclo*octatetraene were prepared by Fries and Pfaffendorf (*Ber.*, 1910, **43**, 212; 1911, **44**, 114) by the self-condensation of coumaranones (IX), the structures, as (X), assigned to them being based on the fact that they were produced by further condensation of dimolecular products.



(IX.)



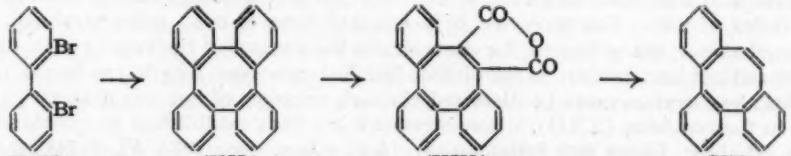
(X.)



(XI.)

It was shown, however, by Baker and Banks (J., 1939, 279) that in the case of the strictly analogous 5-methylcoumaranone the final product had a molecular weight corresponding to that required for a triple condensation product of the simple coumaranone, and hence it must be a derivative of benzene (XI) rather than of *cyclo*octatetraene. There can be no doubt that the similar compounds described by Fries and Pfaffendorf are also tris-coumaronobenzenes. Again, the supposed benz*cyclo*octadienediones prepared by dehydration of 3-benzylidenelævulic acids with acetic anhydride (Sen and Roy, *J. Indian Chem. Soc.*, 1930, **7**, 401) have been shown (Rapson and Shuttleworth, J., 1942, 33) to be otherwise constituted and are almost certainly 2-keto-5-styryl-2 : 3-dihydrofurans. A compound, $C_{48}H_{32}Br_2$, obtained by the action of bromine upon fluorocyclen (probably tetranaphthylene*cyclo*octadiene; Dziewonski and Suknarowski, *Ber.*, 1918, **51**, 457), has been formulated as a derivative of *cyclo*octatetraene (Dziewonski and Susko, *Ber.*, 1925, **58**, 725), but the experimental evidence is insufficient to establish the proposed structure.

The only known cases of genuine *cyclo*octatetraenes are certain benzo-derivatives which have recently been prepared by Rapson and Shuttleworth and their collaborators (Rapson, Shuttleworth, and Niekerk, J., 1943, 326; Shuttleworth, Rapson, and Stewart, J., 1944, 71). Tetraphenylene (1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-tetrabenz-$\Delta^{1:3:5:7}$-*cyclo*octatetraene) was obtained in 16% yield by the action of anhydrous cupric chloride in boiling ethereal solution upon the Grignard reagent derived from 2 : 2′-dibromodiphenyl (XIII), and is a solid, m. p. 233°, which shows the remarkable property of crystallising with half a molecule of solvent of crystallisation from chloroform, carbon tetrachloride, acetone, dioxan, benzene, and pyridine. It is oxidised by chromic acid to tribenz*cyclo*octatetraenedicarboxylic anhydride (XIV), pyrolysis of which with barium hydroxide gives 1 : 2 : 3 : 4 : 5 : 6-tribenz-$\Delta^{1:3:5:7}$-*cyclo*octatetraene (XV).

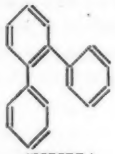


(XIII.) (XII.) (XIV.) (XV.)

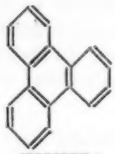
There are two points of general interest about these derivatives of *cyclo*octatetraene, one in connection with their absorption spectra and the other with their molecular geometry (Rapson, Schwartz, and Stewart, J., 1944, 73). The absorption spectrum of tetraphenylene (XII) is extremely similar to that of 2 : 2′-diphenyldiphenyl (XVI), and also to that of tribenz*cyclo*octatetraene (XV). Hence in passing from (XVI) to (XII) the closing of the *cyclo*octatetraene ring causes no marked difference in the absorption spectra, and it may be concluded that no characteristic absorbing system is present in tetraphenylene except that due to the four benzene rings. In marked contrast is the difference between the absorption spectra of 2-phenyldiphenyl

(XVII) and triphenylene (XVIII), where the closure of the six-membered ring causes a completely new type of absorption to appear.

(XVI.)



(XVII.)



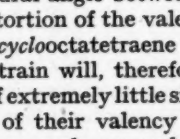
(XVIII.)

(XIX.)

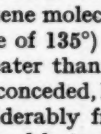
Preliminary examination by *X*-ray analysis and electron diffraction has shown that the molecule of tetraphenylene is not flat. This is to be expected from a molecular model, which when strainless takes the form shown in (XIX), being of a more generally cubic than a planar shape. In the compound itself resonance between the benzene rings will tend to make the molecule somewhat more flat, and a balance will be struck between the increased stability due to such resonance and the decreased stability due to angular deformation of the valencies. The central *cyclo*octatetraene ring is clearly far from being planar, and this may be one of the reasons why it does not show any characteristic aromatic absorption. Indeed the eight-membered ring appears to be merely a space enclosed by the four benzene nuclei, quite unlike the central six-membered ring in the (presumably) planar molecule of triphenylene (XVIII).*

These considerations have some bearing on the possible existence of *cyclo*octatetraene itself. If the molecule is to be a stable aromatic compound behaving as a saturated rather than as an unsaturated compound, then there must be resonance interaction between the bonds, and this is only possible if the molecule is planar, since the structures which contribute to the hybrid can differ only in distribution of the valency electrons and not in the relative positions of the atoms concerned. In passing from one *cyclo*octatetraene structure to the other when the positions of the carbon–carbon double and single bonds are reversed (as in the two Kekulé structures of benzene), considerable movement of the atoms is involved in the least strained structures, so that, if the molecule is to be stabilised by resonance, it must be flat, and automatically becomes to a certain extent rendered instable by strain. To what extent these two effects neutralise each other it is impossible to say, but the molecule would show some tendency to behave like an olefin rather than like the stable molecule of benzene (see Pauling, " Nature of the Chemical Bond," Cornell Univ. Press, 1939, p. 133, footnote; Penney, *Proc. Roy. Soc.*, 1934, *A*, **146**, 223, suggests that the angular strain is enough " to counteract the stabilising influence of resonance ").

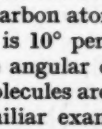
The natural angle between a double and a single bond for a tetrahedral carbon atom is 125°, so that the angular distortion of the valencies in the planar benzene molecule is only 5° for each carbon atom, whereas for the planar *cyclo*octatetraene molecule (internal angle of 135°) the angular distortion is 10° per carbon atom. The total strain will, therefore, be considerably greater than in benzene, where the angular distortions are obviously of extremely little significance. It must be conceded, however, that stable molecules are known which have some of their valency angles bent very considerably from the normal. Familiar examples amongst alicyclic compounds are *cyclo*propane, *cyclo*propene, *cyclo*butane, and *cyclo*butene, in which, however, the rings are easily broken, and in the aromatic series may be mentioned fluorene (XX) and acenaphthylene (XXI).



(XX.)



(XXI.)



(XXII.)

In the case of fluorene (see Hughes, Le Fèvre, and Le Fèvre, J., 1937, 203, and references there cited) the two benzene rings must be inclined at an angle because of the non-identity of the dipole moments of fluorene and certain 2 : 7-disubstituted fluorenes, and even if the molecule is not completely planar the angular strain is probably of the order of 10°. The molecule of acenaphthylene is even more strained, and yet it is an exceedingly stable substance, being formed, for example, by the passage of the vapour of its dihydro-derivative, acenaphthene, over red-hot lead oxide. If the olefinic link has its normal length, the bonds joining this CH:CH group to the naphthalene system must be distorted through an angle of not less than 20°, and the same considerations apply to fluoranthene (XXII), whose structure has been established by synthesis (von Braun and Anton, *Ber.*, 1929, **62**, 145; Fieser and Seligman, *J. Amer. Chem. Soc.*, 1935, **57**, 2174), and which is also so stable as to be produced from its 1 : 2 : 3 : 4-tetrahydro-derivative by oxidation over red-hot lead oxide. These examples make it doubtful if the instability, or even the non-existence, of *cyclo*octatetraene can be explained on the grounds of strain alone.

* Since this lecture was delivered a paper has appeared by Karle and Brockway (*J. Amer. Chem. Soc.*, 1944, **66**, 1974) describing an electron diffraction examination of tetraphenylene. The molecule, models of which are illustrated, is found to be best represented by the form suggested in the lecture, with the centres of the benzene rings lying at the corners of a regular tetrahedron, and with a non-planar eight-membered ring. In a footnote to this paper it is reported that Fieser and Pechet have prepared 1 : 2 : 5 : 6-dibenz-$\Delta^{1:3:5:7}$-*cyclo*octatetraene, and that the two double bonds in the *cyclo*octatetraene ring which are not shared with the benzene rings are olefinic in character.

Fulvenes.—Before leaving the possible monocyclic non-benzenoid aromatic types, mention may be made of the fulvenes (XXIII), whose conjugation, though not completely cyclic, is more perfect than that in *cyclo*heptatriene. The fulvenes, which are generally orange or red, are prepared from *cyclo*pentadiene or derivatives either by condensation with aldehydes or ketones in presence of alkali, or by treatment with a Grignard reagent, giving the magnesium derivative (XXIV), followed by reaction with an aldehyde or ketone to give the tertiary alcohol (XXV) and dehydration over alumina at 250° to give the fulvene (XXIII).

(XXIII.)

(XXIV.)

(XXV.)

(XXVI.)

(XXVII.)

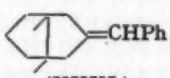
Although the fulvenes are chemically reactive, they do not rearrange to the isomeric benzene derivatives; thus benzfulvene (XXVI) does not rearrange to naphthalene at 250° over alumina, and dibenzfulvene (XXVII) has shown no tendency to rearrange to phenanthrene (Wieland, Reindel, and Ferrer, *Ber.*, 1922, **55**, 3317). These facts suggest that such molecules possess moderate resonance energy, but no determination of the value of this energy in a fulvene has been recorded.

Pentalene.—This is the simplest bicyclic aromatic system which might exist, if derivatives of *cyclo*butadiene are excluded. It consists of two fused five-membered fulvene rings, a structure in which two arrangements of the double bonds are possible, (XXVIII) and (XXIX), but the central bond remains single.

(XXVIII.)

(XXIX.)

(XXX.)



(XXXI.)

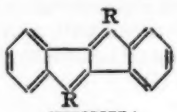
This compound was first postulated as a possible aromatic type by Armit and Robinson (J., 1922, **121**, 828), and the name " pentalene " is suggested for it in Patterson and Capell's " The Ring Index " (1940, p. 110). In view of its similarity to naphthalene attempts were made by Barrett and Linstead (J., 1936, 612) to obtain this hydrocarbon by dehydrogenation of *cis*-0 : 3 : 3-*bicyclo*octane (XXX) in the vapour phase over platinum, but the compound was recovered unchanged under conditions which resulted in the dehydrogenation of decalin to naphthalene. An attempt was also made to dehydrogenate 2-benzylidene-*cis*-0 : 3 : 3-*bicyclo*octane (XXXI) to a derivative of pentalene by means of selenium at 300—330°, but it was partly unchanged and partly decomposed, although in control experiments 2-benzyl-*trans*-octalin was smoothly converted into 2-benzylnaphthalene. Barrett and Linstead conclude that " these results, although negative, provide some experimental support for the view that naphthalene is a unique dicyclic hydrocarbon and that the *bicyclo*octatetraene (XXVIII) does not possess aromatic characteristics."

The little evidence available certainly indicates that pentalene is not a stable aromatic system, and it is difficult to suggest adequate reasons for this. Attention may be drawn, however, to three considerations. First, in pentalene there are only four electrons not necessarily involved in co-valency formation in each ring, whereas in typical benzenoid compounds there are six. Secondly, pentalene is a derivative of fulvene, and the fulvenes as a class are instable, showing a marked tendency to polymerise and to undergo autoxidation. Thirdly, on the simple strain theory based on the tetrahedral carbon atom pentalene should be a moderately strained molecule (internal angles of 108° for a *regular* pentagon, instead of 125° for the angle between a double and a single bond about a carbon atom, although the latter value might be slightly reduced because one angle in each pentagon should be 110°), but recent work on heats of hydrogenation has made it very doubtful if such considerations apply in the case of monocyclic five- and six-membered ring compounds. Classical theory predicts that introduction of one or two double bonds into *cyclo*pentane should result in a more strained and less stable molecule than when the double bonds are introduced into the molecule of *cyclo*hexane, and that in consequence the heats of hydrogenation of *cyclo*pentene and *cyclo*pentadiene should be greater than those of *cyclo*hexene and $\Delta^{1:3}$-*cyclo*hexadiene respectively. Direct measurements of the heats of hydrogenation by Kistiakowsky and his collaborators (*J. Amer. Chem. Soc.*, 1935, **57**, 65,876; 1936, **58**, 137,146; 1937, **59**, 831; see also Taylor, *Ann. Reports*, 1937, **34**, 214) have shown that, although the differences in values for the five- and six-membered rings are not great, the values themselves are unmistakably larger in the case of the hexane derivatives, and it must be concluded that the five-membered ring becomes more stable with increasing unsaturation.

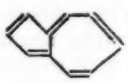
A few complex molecules containing the dibenzopentalene system have been made by Brand (*Ber.*, 1912, **45**, 3071; Brand and Ludwig, *ibid.*, 1920, **53**, 809; Brand and Hoffmann, *ibid.*, p. 815; Brand and Müller, *ibid.*, 1922, **55**, 601; Brand, Gabel, and Ott, *ibid.*, 1936, **69**, 2504; Wawzonek, *J. Amer. Chem. Soc.*, 1940, **62**, 745). These are diphensuccindadienes of type (XXXII; R = Ph or Cl), brown substances obtained from diphensuccindandione either by treatment with aryl Grignard reagents and dehydration of the resulting ditertiary alcohols, or by treatment with phosphorus pentachloride and elimination of two molecules of hydrogen chloride.

The aromatic system consisting of fused five- and seven-membered rings (XXXIII) is found in the azulenes, and may be regarded as the next aromatic homologue of pentalene. The azulenes are compounds of considerable stability, which is in marked contrast with the apparent instability of pentalene. Two points may be

made in this connection; first, the azulene molecule may be in part less strained than that of pentalene because the internal angles of a regular heptagon are 128·6°, which is very close to 125°, and secondly, the seven-membered



(XXXII.)

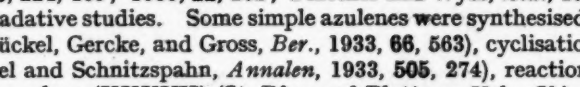

(XXXIII.)

(XXXIV.)

ring contains three pairs of doubly bound carbon atoms and, therefore, has six " free " electrons. It follows that, if these two points are valid, then the system consisting of two fused seven-membered rings containing six double bonds (XXXIV) should show aromatic stability, but as yet compounds of this type are unknown.

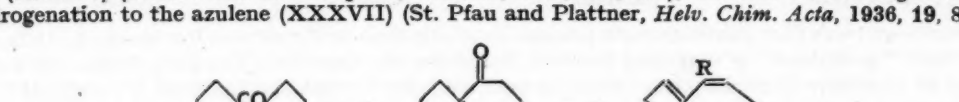
Azulenes.—The azulenes contain the fused five- and seven-membered ring aromatic system (XXXIII), and are isomeric with the naphthalenes. They are sufficiently well known not to require detailed description here; two reviews are available, one by Haworth (*Ann. Reports*, 1937, **34**, 393) and the other by Arnold (*Die Chemie*, 1943, **56**, 7).

The azulenes are blue, violet, or green hydrocarbons present in certain essential oils or obtained from them by high-temperature dehydrogenation, and are separated from the resulting mixtures by taking advantage of their solubility in concentrated aqueous phosphoric acid, from which solutions they separate on dilution with water (Sherndal, *J. Amer. Chem. Soc.*, 1915, **37**, 167, 1537). They form picrates and complexes with *s.*-trinitrobenzene. Their structure has been established largely by the work of St. Pfau and Plattner (*Helv. Chim. Acta*, 1936, **19**, 858; 1937, **20**, 224, 469; 1939, **22**, 202; Plattner and Wyss, *ibid.*, 1940, **23**, 907; 1941, **24**, 483) both by synthetical and degradative studies. Some simple azulenes were synthesised from octalin by ozonolysis to the diketone (XXXV) (Hückel, Gercke, and Gross, *Ber.*, 1933, **66**, 563), cyclisation to the *cyclo*pentenocycloheptenone (XXXVI) (Hückel and Schnitzspahn, *Annalen*, 1933, **505**, 274), reaction with a Grignard reagent, and dehydrogenation to the azulene (XXXVII) (St. Pfau and Plattner, *Helv. Chim. Acta*, 1936, **19**, 858).



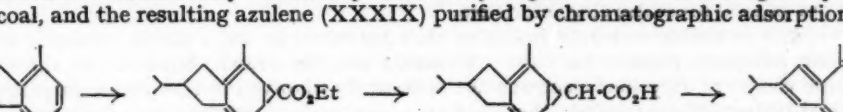
(XXXV.) (XXXVI.) (XXXVII.)

Several alkylated azulenes have also been prepared by another ingenious method due to St. Pfau and Plattner (*locc. cit.*; also Wagner-Jauregg and Hippchen, *Ber.*, 1943, **76**, 694). Hydrindene or an alkylated hydrindene is heated with diazoacetic ester, a pseudophenylacetic ester (XXXVIII) thereby being obtained. This is hydrolysed and then simultaneously decarboxylated, dehydrogenated and rearranged by heating with palladium–charcoal, and the resulting azulene (XXXIX) purified by chromatographic adsorption on alumina.



(XXXVIII.) (XXXIX.)

The fused five- and seven-membered ring system has been proved to be present in the naturally occurring reduced azulene derivative β-vetivone (XL), which yields vetivazulene (XXXIX) on dehydration and dehydrogenation. Controlled degradation processes have yielded on the one hand a derivative of *cyclo*pentane (XLI), and on the other hand a derivative of *cyclo*heptane (XLII) (St. Pfau and Plattner, *Helv. Chim. Acta*, 1940, **23**, 768).

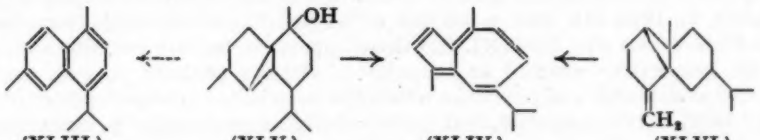


(XLI.) (XL.) (XLII.)

The azulenes are compounds of considerable stability, as is evident from their usual method of formation, and there is, as yet, no clear evidence that they may be converted into the isomeric naphthalenes. Nevertheless the azulenes appear to be physically less stable than the isomeric naphthalenes. Perrottet, Taub, and Briner (*Helv. Chim. Acta*, 1940, **23**, 1260) have determined the heats of combustion of the two isomeric compounds cadalene (XLIII), and guaiacazulene (XLIV), and find that the former value is 29·5 kg.-cals. per g.-mol. lower than the latter. From this it has been calculated that the total bonding energy of azulene itself is 8% less than the total bonding energy of naphthalene, and that the resonance energy of azulene is of the order of 45 kg.-cals. per g.-mol., compared with the resonance energy of naphthalene, which is 75 kg.-cals. per g.-mol.

In view of this fact it is curious that the tricyclic terpene ledol (Komppa and Nyman, *Compt. rend. Trav. Lab. Carlsberg*, 1938, **22**, 272) (XLV), which contains the carbon skeletons of both cadalene (XLIII) and guaiacazulene (XLIV), should be dehydrogenated with rupture of the *cyclo*propane ring to give mainly guaiac-

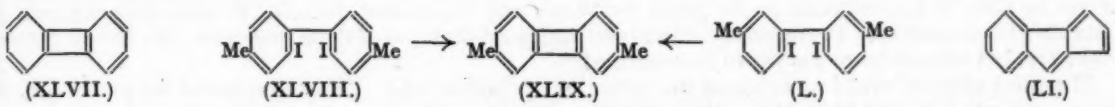
azulene and relatively little cadalene. A similar case is afforded by aromadendrene (XLVI) (Radcliffe and Short, J., 1938, 1200; Naves and Perrottet, *Helv. Chim. Acta*, 1940, **23**, 912), which is dehydrogenated to give guaiacazulene and not a derivative of naphthalene.



(XLIII.) (XLV.) (XLIV.) (XLVI.)

" *Diphenylene.*"—Diphenylene (also called biphenylene and *cyclo*butadibenzene) is the tricyclic hydrocarbon (XLVII), isomeric with acenaphthylene, which has been regarded for a long time as a possible aromatic type. Five arrangements of the bonds are possible, four dibenzenoid in character, and one doubly ortho-quinonoid.

The hydrocarbon has an interesting history. Hosaeus in 1893 (*Monatsh.*, **14**, 323) attempted to prepare it by the action of sodium on *o*-dibromobenzene, but obtained instead a trace of benzene, a little diphenyl and a mixture of complex products. Niementowski (*Ber.*, 1901, **34**, 3331) treated the diazonium salt derived from 2 : 2′-diaminodiphenyl with copper powder, but the product was carbazole. The dehydration of 2-hydroxydiphenyl to diphenylene was unsuccessfully attempted by Cullinane, Morgan, and Plummer (*Rec. Trav. chim.*, 1937, **56**, 627). The preparation of diphenylene from 2 : 2′-dibromodiphenyl in almost theoretical amount by the action of sodium in boiling ether was claimed by Dobbie, Fox, and Gauge (J., 1911, **99**, 683; 1913, **103**, 36). It was described as closely resembling diphenyl but had a higher melting point (74·5—75°; diphenyl, 70·5°); it was extremely volatile and concordant results for the analyses were only obtained by carrying out the combustions under abnormally vigorous conditions. The three selected analyses and the molecular weight determinations are in fair agreement with the formula $C_{12}H_8$. The hydrocarbon was not attacked by cold alkaline permanganate, but hot chromic acid mixture gave phthalic and benzoic acids. Bromination gave 2 : 2′-dibromodiphenyl and a dibromodiphenylene giving *p*-bromobenzoic acid on oxidation. The nature of this hydrocarbon remains obscure, and its preparation has not been successfully repeated in spite of many attempts. Complete failure has been reported by Mascarelli and Gatti (*Gazzetta*, 1933, **63**, 661), by Rapson and Shuttleworth (J., 1941, 487), and by Lothrop (*J. Amer. Chem. Soc.*, 1941, **63**, 1187), although a variety of experimental conditions was used, including the replacement of sodium by potassium, and the dibromodiphenyl by the corresponding dichloro- and di-iodo-derivatives.



(XLVII.) (XLVIII.) (XLIX.) (L.) (LI.)

Lothrop (*loc. cit.*), having failed to repeat the earlier claim, finally succeeded in preparing a compound $C_{12}H_8$ in 5% yield by distilling 2 : 2′-dibromodiphenyl or, better, 2 : 2′-di-iododiphenyl with cuprous oxide, steam-distilling the product, and purifying the substance as its scarlet picrate. The hydrocarbon was finally liberated from the picrate by sublimation at 100°, and obtained in light-yellow prisms, m. p. 110°, which was shown by analysis and molecular weight determination to be undoubtedly $C_{12}H_8$. The substance is not identical with the compound described in 1911, nor with acenaphthylene, and is claimed by Lothrop as diphenylene (XLVII). Oxidation with chromic acid gave some phthalic acid (yield unstated), and by passage as a vapour with hydrogen over hot copper it was one-third converted into diphenyl and two-thirds unchanged. The stability and colour of its picrate are consistent with a tricyclic aromatic hydrocarbon (see Basil and Hauber, *J. Amer. Chem. Soc.*, 1931, **53**, 1090), as is also its absorption spectrum (Carr, Pickett, and Voris, *ibid.*, 1941, **63**, 3231). Lothrop also brought forward evidence in favour of the symmetrical structure of the molecule. 2 : 2′-Di-iodo-4 : 4′-dimethyldiphenyl (XLVIII) and 2 : 2′-di-iodo-5 : 5′-dimethyldiphenyl (L) were each converted into a " diphenylene," and the products from both reactions were identical, being regarded as 2 : 7-dimethyldiphenylene (XLIX). A later paper by the same author (*J. Amer. Chem. Soc.*, 1942, **64**, 1698) described two other diphenylenes, the 1 : 8-dimethyl- and the 2 : 7-dimethoxy-derivatives.

Two novel features are involved in the diphenylene formulæ for these compounds. First, they may be regarded as derivatives of the unknown substance *cyclo*butadiene, and secondly they contain a four-membered ring fused to a benzene nucleus. With regard to the first point there is evidence to suggest that the *cyclo*butadiene ring may be stabilised by fusion with the benzene nuclei. The second point is more difficult, because there appears to be no established case in chemical literature of a compound containing fused aromatic and four-membered rings, a subject which is discussed in a separate section (p. 266). Such molecules would have bonds attached to the aromatic nucleus strained through angles of 30°; in the case of diphenylene (XLVII) four bonds would be strained to this large extent and it might be expected that the resulting strain would confer a considerable degree of instability upon the molecule, whereas the actual " diphenylenes " are very stable, being formed by high temperature reactions, and behaving as typical aromatic compounds.

The preparation of the hydrocarbon $C_{12}H_8$ by Lothrop's method has been confirmed (Baker, Grice, and Donne, unpublished observations; Baker, *Nature*, 1942, **150**, 210) and it was reported that mild catalytic

reduction resulted in the uptake of approximately three molecules of hydrogen, giving a volatile oil, and that it behaved as a saturated compound and exhibited no acetylenic properties. The same hydrocarbon has also been prepared in 4% yield by Rapson, Shuttleworth, and Niekerk (*loc. cit.*; Rapson and Shuttleworth, *loc. cit.*) by treating the Grignard reagent prepared from 2 : 2'-dibromodiphenyl with dry cupric chloride (method due to Krizewsky and Turner, J., 1919, **115**, 560), a reaction which simultaneously yields tetraphenylene (see p. 261).

Apart from the diphenylene structure (XLVII) there appears to be only one alternative for a hydrocarbon $C_{12}H_8$ possessing the properties described and capable of yielding phthalic acid on oxidation. This is the structure (LI), the benzo-derivative of pentalene which has been called *cyclo*pentindene (Patterson and Capell, "The Ring Index," 1940). The suggestion that Lothrop's diphenylene might be *cyclo*pentindene was made in 1942 (Baker, *loc. cit.*), thus avoiding the two difficulties inherent in the diphenylene formula which have already been mentioned. On general grounds (LI), for which three arrangements of the bonds are possible, two benzenoid and one ortho-quinonoid, would be expected to be a stable, almost strainless molecule of aromatic type. Coulson (*Nature*, 1942, **150**, 577) has calculated that the resonance energies of diphenylene and *cyclo*pentindene differ by only about 4 kg.-cals., the former being the greater, but that diphenylene possesses a strain energy of possibly 100 kg.-cals., whereas the strain energy of *cyclo*pentindene is only a few kg.-cals., and concludes that *cyclo*pentindene should be considerably more stable than diphenylene.

At the time when the *cyclo*pentindene structure was put forward as an alternative to the diphenylene formula all the known facts were capable of explanation on the basis of either structure. Even the production of the same dimethyl derivative from structurally isomeric di-iododiphenyls may be accounted for by assuming that under the vigorous conditions of the reaction one of the benzene rings undergoes rupture at the bond common to the benzene and the four-membered ring (Baker, *loc. cit.*). More recently, however, three pieces of evidence have become available which give strong support to the diphenylene structure. Waser and Schomaker (*J. Amer. Chem. Soc.*, 1943, **65**, 1451), in an electron diffraction investigation of diphenylene, find inter-atomic distances of 1·42 A. (very strong), 2·44 A. (strong), 2·78 A. (strong), corresponding to the average bonded C–C distances, the *meta*- and *para*-distances in the benzene ring respectively, and 2·1 A. (very weak) regarded as the diagonals of the four-membered ring. These authors state that the *cyclo*pentindene structure is definitely excluded, because there are no C–C distances of 2·30 A. corresponding to the calculated diagonals of two regular pentagons. The validity of this assertion rests upon assumptions as to the dimensions of the two five-membered rings. These will not be regular, because, for example, the bond common to the two is wholly single, so that some of the diagonals may equal the distance between *meta*-carbon atoms in the benzene ring. The absence of any indication of a distance of the order of 2·30 A. is, however, scarcely consistent with the *cyclo*pentindene structure. A preliminary note of an incomplete *X*-ray crystallographical investigation of Lothrop's hydrocarbon by Chia-Si Lu (included in the paper by Waser and Schomaker, *loc. cit.*) shows a complex unit cell containing six molecules. Provisionally it has been suggested that two of these molecules may have a centre of symmetry, but this evidence has yet to be confirmed.*

The third piece of evidence concerns the reduction of diphenylene. It was suggested by Baker (*loc. cit.*) that a molecule possessing the diphenylene structure should undergo ready catalytic reduction with rupture of the strained four-membered ring to give diphenyl, and it was stated that in fact the compound combines with approximately three molecules of hydrogen. This statement was based on catalytic reduction experiments in acetic acid at room temperature in presence of a palladium–charcoal catalyst, and these experiments have since been confirmed. It has been found, however (unpublished experiments), that the course of the reduction is quite different when hydrogenation is effected in alcoholic solution in presence of Raney nickel; the uptake of hydrogen is rapid and ceases after little more than one molecule of hydrogen is absorbed, and an 85% yield of pure diphenyl can be isolated from the product. It is difficult to imagine how *cyclo*pentindene could so readily yield diphenyl, as the reaction involves the breaking of two presumably strainless C–C links and the formation of a new C–C link.

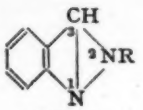
The balance of evidence is thus definitely in favour of the original diphenylene structure for Lothrop's hydrocarbon. If future work confirms this conclusion, diphenylene will have to be regarded as a unique type of molecule, in which the butadiene structure is stabilised by fusion with the two benzene rings, just as the *cyclo*octatetraene structure may be stabilised by fusion with three or four benzene rings, and in which the expected instability due to strain is compensated by increased stability due to resonance. It is probably also the only type of molecule in which it is possible to have an aromatic nucleus fused to a four-membered ring.

Non-existence of Compounds containing a Four-membered Ring fused to an Aromatic Nucleus.—Many formulæ are to be found in chemical literature in which an aromatic nucleus is shown fused to a four-membered ring. These fall broadly into three types, (1) tricyclic benzenoid compounds such as anthracene, acridine, phenazine, etc., (2) bicyclic compounds containing nitrogen with a bridged five-membered ring fused to a benzene ring, such as anthranil, 2-alkylindazoles, etc., and (3) a number of compounds of quite unrelated types. It would not be profitable to discuss individual cases in the last category; most of the suggested four-membered ring structures are advanced without experimental justification, and in some cases the work is of doubtful value and a knowledge of the molecular weight of the compound is lacking. Sometimes a dipolar molecule is represented as completely covalent, and in one instance the four-membered ring is only made possible by the

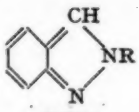
* Note added, April 30th, 1945. The complete *X*-ray crystallographical analysis of diphenylene has now become available (Waser and Chia-Si Lu, *J. Amer. Chem. Soc.*, 1944, **66**, 2035). The results establish conclusively the structure of the compound as (XLVII).

inclusion in the formula of two quinquevalent carbon atoms. In all these cases the onus of proof rests with those who suggest the formulæ.

(LII.)



(LIII.)



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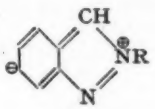
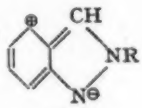


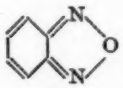
(LV.)



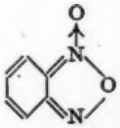
(LVI.)

With regard to type (1), anthracene, acridine, and related molecules were at one time written with long covalent links joining the central atoms of the system, thus making two four-membered rings as in (LII). The *X*-ray investigation of anthracene crystals by Robertson (*Proc. Roy. Soc.*, **1933**, *A*, **140**, 79) has shown that the three hexagons are completely regular, so that the central atoms cannot be covalently linked. Further evidence on this point is that if the structure of anthracene were (LII), then its resonance energy would be simply that due to the two isolated benzene rings, namely $2 \times 39 = 78$ kg.-cals., whereas it is actually but little less than three times the value for benzene, namely, 105 kg.-cals. These molecules are clearly hybrid and may be written with four arrangements of the double bonds corresponding to the most stable structures which contribute to the normal state of the molecule (see Pauling, "The Nature of the Chemical Bond," Cornell University Press, 1939). It has thus rightly become customary to write these anthracene-like molecules without the central bond.

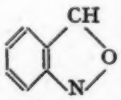
Bicyclic compounds of type (2) have been represented as containing either a four-membered ring as shown in formula (LIII) for a 2-substituted indazole, or else as being ortho-quinonoid in structure as shown in formula (LIV). The 2-alkyl- or 2-aryl-indazoles do not appear to possess the characteristics of genuine ortho-quinonoid compounds, such as colour and ability to add two molecules of bromine, and there can be little doubt that the molecules are resonance hybrids composed of the neutral orthoquinonoid form and not less than thirty-six additional dipolar forms, of which two are shown in formulæ (LV) and (LVI). If for simplicity it is assumed that these dipolar forms all contribute equally to the hybrid, the distribution of the charges is found to be such that the nitrogen atom in position 2 bears a certain positive charge, nitrogen atom 1 and carbon atoms 3 each bear one-fifth, and the six carbon atoms of the benzene nucleus each bear one-tenth of the corresponding negative charge. The result is that the molecule is stabilised by resonance to such an extent that it shows aromatic stability, and there is no need to assume the presence of the four-membered ring. As in the case of anthracene, the real state of the molecule cannot be represented by a single formula, and the determination of the actual resonance energy of such molecules and of the interatomic distances in the five-membered rings would be of very considerable interest.



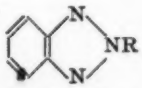
(LVII.)



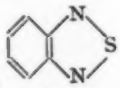
(LVIII.)



(LIX.)



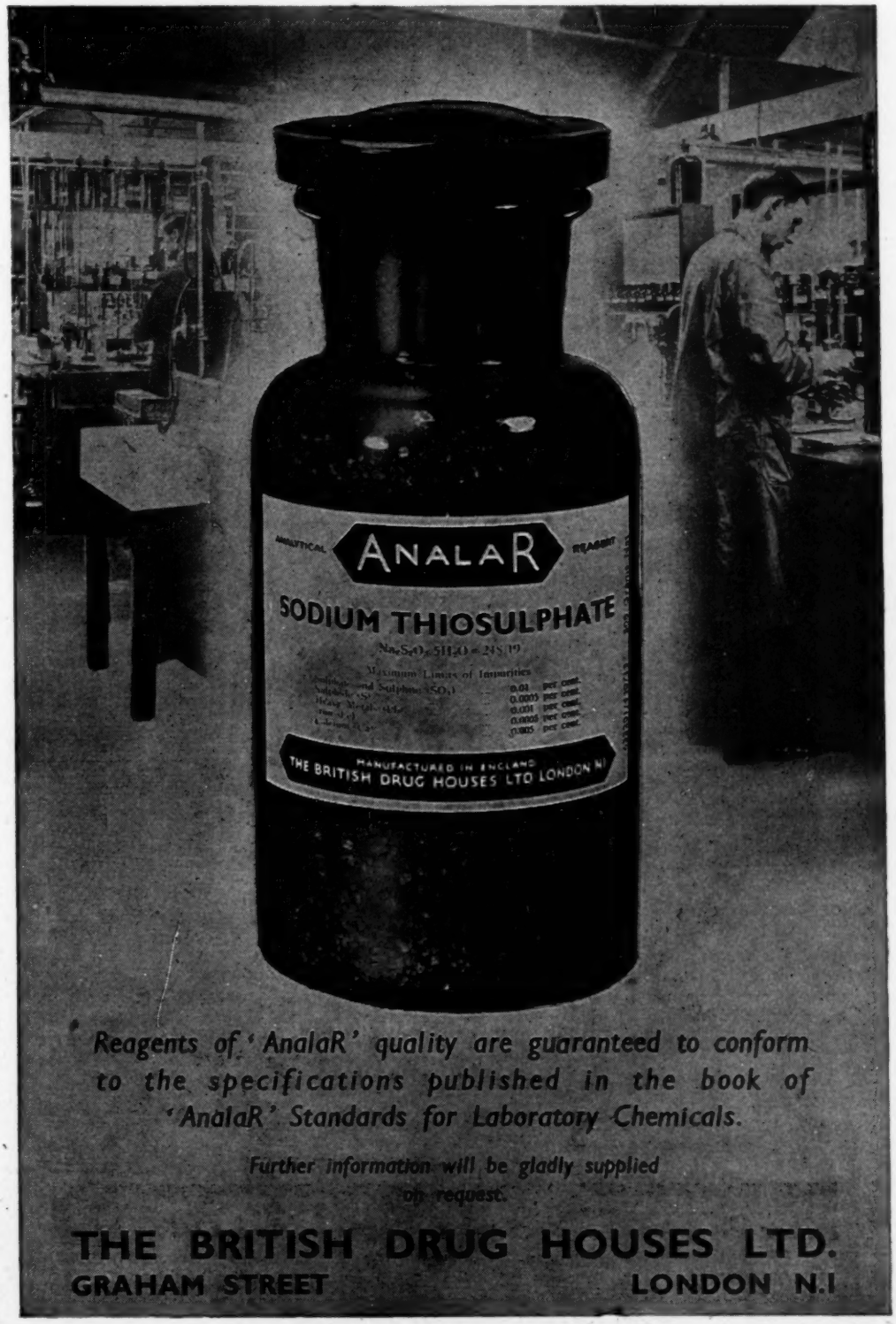
(LX.)



(LXI.)

There is evidence that certain molecules of this kind, all of which possess the same resonance possibilities, are much closer to genuine ortho-quinonoid types than others. This is the case with benzfurazan (LVII) and benzfurazan oxide (LVIII), which were at one time written with four-membered rings. These compounds behave like *o*-quinones in that they combine additively with two molecules of bromine, addition occurring at the olefinic bonds of the six-membered ring, and are, therefore, best represented by the formulæ shown (Hammick, Edwardes, and Steiner, J., **1931**, 3308), but the rather slow rate of addition indicates some departure from the fixed ortho-quinonoid structure. The majority of molecules of this type which have been written with four-membered rings are, however, of a more hybrid character; they include anthranil (LIX; in this and the two succeeding formulæ no attempt is made to indicate the distribution of the valency electrons in the five-membered rings, and the benzene nucleus is shown as aromatic), *C*-methylanthranil, and anthranilcarboxylic acid (anthroxanic acid), thioanthranil, 2-substituted benztriazoles (LX), piazthiole (LXI), and piazselenole.

Further evidence which shows that compounds possessing a four-membered ring fused to an aromatic nucleus are at least not easy to prepare is to be found in a study of reactions where such a ring system might be produced. For example, dehydration of salicylic acid does not give a four-membered ring anhydride, but disalicylide containing an eight-membered ring, tetrasalicylide containing a sixteen-membered ring, and polysalicylides; some derivatives of salicylic acid are known to behave similarly. Phenol-*o*-sulphonic acids give not intramolecular but intermolecular anhydrides; anthranilic acid yields only intermolecular amides, and similar cases could be cited. The action of sodium on *o*-xylylene dibromide (Baker, Banks, Lyon, and Mann, J., 1945, 27) gives the centro-symmetric form of 1 : 2 : 4 : 5-dibenz-$\Delta^{1:5}$-*cyclo*octadiene, 1 : 2 : 5 : 6 : 9 : 10-tribenz-$\Delta^{1:5:9}$-*cyclo*dodecatriene, and polymeric products.



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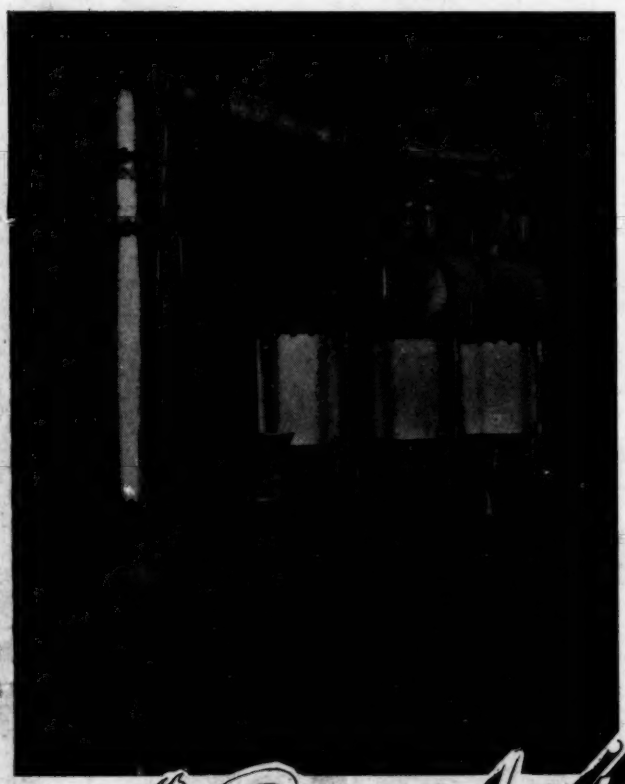

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